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THE THERAPEUTIC USE OF ANTITOXIN IN EXPERIMENTAL TETANUS*

HARRIS B. SHUMACKER, JR., M.D., WARFIELD M. FIROR, M.D., AND
AUSTIN LAMONT, M.D., BALTIMORE, MD.

(From the Surgical Hunterian Laboratory, the Johns Hopkins University)

THE widespread prophylactic use of tetanus antitoxin has very effectively reduced the incidence of clinical tetanus. The results during the last World War, furthermore, proved conclusively that tetanus ensuing after the prophylactic administration of antitoxin tends to be mild in character, with a long period of incubation and a lowered mortality.¹ The introduction of active immunization with tetanus toxoid on a large scale undoubtedly will further decrease the occurrence of this disease. Nevertheless, cases still occur and the problem of treatment remains an important and to a large degree an unsolved one.

Recent studies have put the pathogenesis of tetanus on a sound basis and have made the problem of treatment more rational than formerly. Serious doubt has been cast upon the nerve carriage theory which has long dominated the experimental literature and which has so influenced the clinical concept of the disease and of its treatment.²⁻⁶ Tetanus, in our view, is a disease with dual manifestations: (1) stiffness or rigidity of muscles due to the direct action of the toxin upon the peripheral nerve organs in muscle tissue and (2) reflex spasms due to the action of toxin on the motor cells of the central nervous system. Local tetanus is characterized by the local spread of toxin through a muscle or groups

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of antitoxin in the blood-vascular system of an animal against tetanus toxin in general and specifically against toxin introduced by various routes. We were also desirous of learning whether the efficacy of antitoxin varied in tetanus-sensitive and tetanus-resistant species. We shall summarize the results of these studies.^{14*}

The protecting value of antitoxin varies, for some unknown reason, in different species. Antitoxin is less effective in the very tetanus-sensitive guinea pig than in the slightly less sensitive mouse and is still less effective than in the tetanus-resistant dog and cat; and yet the variation is not directly proportional to the sensitivity or resistance of the species. It cannot be accounted for on the basis of the difference in the lethal dose in the various species, nor on the basis of difference in concentration of the antitoxin. This relative inefficiency of antitoxin in protecting against toxin in sensitive animals (man is probably of the same order of sensitivity as the guinea pig and the monkey) is of no real consequence as far as its clinical application is concerned, for the same effect can be easily obtained by giving a sufficiently large amount of antitoxin.

A given amount of antitoxin will protect against from two to eight times more toxin if the two are mixed *in vitro* before injection than if they are delivered directly into the blood stream. This we interpret as meaning that, given a certain amount of toxin and a slight excess of antitoxin (as measured by the "in vitro protecting value") in the blood of an animal, each molecule of toxin is not completely neutralized *instantly*, thus affording an opportunity for some molecules of toxin to escape into the central nervous system (and other tissues) where fixation and perhaps alteration may occur so rapidly that they cannot become neutralized unless there is a sufficient excess of antitoxin. Abel and his co-workers¹² have demonstrated that some of the toxin which finds its way into the blood stream of animals passes rapidly out of it and becomes fixed in the tissues in an unrecoverable state. They¹³ presented evidence to support their suggestion that fixed toxin actually can be neutralized, provided, however, that the antitoxin is available before a certain portion of the incubation period has elapsed and provided that a large excess of antitoxin is present.† In speaking of toxin which is circulating in the blood-lymph system, Abel and Chalian¹³ state that it is as completely and easily neutralized by injected antitoxin as would be the case in an *in vitro* experiment. Although our experiments would indicate that this statement is not quantitatively true, it is absolutely correct in principle, since the toxin requires only a sufficient amount of antitoxin for its speedy and complete neutralization.

*In these studies the antitoxin was given intravenously immediately before the toxin was injected.

†This observation is opposed to the concepts of earlier workers who believed that no fixed toxin could be neutralized by antitoxin.¹⁹⁻²¹

of contiguous muscles with poisoning of the nerve end organs and consequent stiffness. The rigidity of the musculature in general tetanus is due to the diffuse distribution of the toxin by way of the blood stream to the end organs of many voluntary muscles. The convulsive manifestations of the disease and in most cases death are due to the deposition of blood-borne toxin in the central nervous system.²⁻¹⁰ Since the toxin is distributed throughout the body and into the central nervous system by the blood-lymph system, it is obvious that the direct blocking of peripheral nerves with antitoxin as advised long ago by von Behring¹¹ has no rational basis. The demonstration in experimental animals by Abel and his associates^{12, 13} that antitoxin has no therapeutic effect, once a lethal amount of toxin has been fixed by the body tissues and the period of incubation has passed, has made it clear why certain patients with tetanus are apparently beyond help. The theory of the alteration of tetanus toxin in the central nervous system into a new lethal agent and the inefficacy of tetanus antitoxin, once a fatal dose of toxin has been fixed in the cord or brain stem and symptoms have developed, likewise point to the futility of treatment in such cases.^{8, 10} But, since there is no method by which we can determine whether a given patient with tetanus has or has not already fixed a lethal amount of toxin, we must continue to treat actively all patients in the hope of curing those who are not already doomed and who might otherwise die.

In an effort to understand better the action of tetanus antitoxin, we have been engaged for several years in a series of experiments. Certain of these have been previously described.¹⁰ Others dealing with the protecting value of antitoxin against toxin introduced by various routes will be reported in detail shortly,¹⁴ together with a full discussion of related problems. In the present communication we shall first discuss some of these general problems relating to antitoxin and shall then present fully some studies concerning the best mode of administration of antitoxin as a therapeutic agent.

GENERAL CONSIDERATIONS

Tetanus antitoxin is standardized in this country in terms of the American unit. One American unit of tetanus antitoxin is, by definition, ten times that amount of antitoxin which, when mixed in vitro for one hour with a standard test dose of toxin (equivalent to 100 minimal lethal doses) and then injected subcutaneously, will for four days prevent the death of a 350 Gm. guinea pig.* The standardization of antitoxin is on a sound basis and is especially accurate in this country where a single test toxin is employed.¹⁶⁻¹⁸ But the simple definition of the antitoxic unit tells us little or nothing of the behavior of antitoxin in the animal body. We were especially anxious to know the relative efficacy

*Control studies are done simultaneously with a standard antitoxin of known strength.

We have suggested²² that natural resistance to tetanus may depend upon the species ability to prevent the fixation within the central nervous system of an amount of toxin which will cause death.* Certain considerations, furthermore, make it appear plausible that a similar important mode of action may be utilized in acquired active and passive immunity.

Once tetanus toxin is being deposited in the central neurons the great problem is its neutralization before it has become fixed or altered or during the early phase of fixation when it is still neutralizable. In contrast with this very difficult problem we have demonstrated that free toxin in the skin, subcutaneous tissues, muscles, or blood is readily and completely neutralized by the simple administration of a sufficient quantity of antitoxin intravenously.† What is the best manner of bringing as much antitoxin as possible as quickly as possible to the central nervous system?

EXPERIMENTS CONCERNING THE BEST METHOD FOR THE THERAPEUTIC ADMINISTRATION OF TETANUS ANTITOXIN

Experiment 1 (Table I).—Twenty-one hours after the injection of 2 G-P LD50's of tetanus toxin into the thigh muscles of guinea pigs, varying amounts of antitoxin were injected into the cisterna in one group and into a vein in another. In the group in which the animals received antitoxin by intracisternal injection only the single animal which received 1 unit of antitoxin died, and all those which received 2 or more units survived. In contrast to this, only those animals in the group receiving antitoxin intravenously which were given 20 units or more lived. When the administration of antitoxin was delayed until twenty-three hours after injection of the toxin, at a time when the local tetanus was approximately of the same degree as in the preceding part of the experiment, half of those animals which received 1 to 2 units of antitoxin into the cisterna survived and 83 per cent of those which received 10 to 50 units. Of those which were given antitoxin intravenously only the one which received 100 units survived. In a third group treated with similar amounts of antitoxin given intramuscularly none survived. When treatment was instituted twenty-eight hours after

*Wolff-Eisner had previously suggested a similar idea.²³ Roux and Borrel²⁴ from their experience with "cerebral tetanus" and from studies with diphtheria toxin in rats and morphine in rabbits made the same suggestion. Inadvertently, reference to the latter was omitted in our original communication.

†Our experiments mentioned up to this point deal largely with the protection against toxin afforded by antitoxin given immediately before the injection of toxin and by the intravenous route. Antitoxin given intravenously was found to give better prophylactic protection than antitoxin given by other routes. In guinea pigs and in dogs we have found that antitoxin injected into the cisterna is less efficient than antitoxin given intravenously in protecting against toxin introduced immediately afterwards, either into a vein or into a muscle. Furthermore, although no complete investigation on this point was undertaken, a few observations suggest that antitoxin given subcutaneously or intramuscularly is less effective than that given intravenously. This is as might be expected, for toxin injected by any of these routes is absorbed into the blood stream and should be more quickly and effectively reached by antitoxin injected directly into the blood than by antitoxin placed elsewhere.

Antitoxin introduced intravenously is less effective against toxin deposited subcutaneously, intramuscularly, or intradermally than it is against toxin injected into the blood stream. Although clinically toxin is generally liberated in the subcutaneous or intramuscular tissues, our observations again give little cause for concern in clinical cases for, although antitoxin is slightly less efficacious against toxin in these tissues than against that circulating in the blood stream, an excess of antitoxin neutralizes the toxin completely and effectively.

With regard to the protecting value of antitoxin injected into a vein against toxin introduced directly into the cord, we found that an entirely different situation exists. If toxin is placed directly into the lumbar cord of dogs, it takes over 8,000 times more antitoxin (injected intravenously immediately before the toxin is injected) to prevent death than if the toxin had been injected into the blood stream, and about 3,500 times more antitoxin than if the toxin had been placed in the muscle. We have previously reported similar experiments.¹⁰ Furthermore, we have shown that far greater amounts are necessary if the administration of antitoxin is delayed for some time after the deposition of toxin in the cord and that, if the interval is prolonged until symptoms have intervened, even enormous doses of antitoxin will not save the animal.

The problem of neutralization of toxin within the cord is simply a matter of bringing to these poisoned tissues soon enough a sufficient quantity of antitoxin.¹⁰ For example, to prevent the appearance of symptoms in the dog after the injection of a fatal quantity of toxin into the medulla, it suffices, if the administration of antitoxin is delayed five hours after giving the toxin, to place into the same area in the medulla 800 times as much antitoxin as could have sufficed to neutralize that toxin had it and the antitoxin been injected simultaneously into the blood stream; whereas, if the antitoxin is injected into the blood stream instead of into the medulla, 800,000 times as much antitoxin is required as would have sufficed had both been placed in the blood stream. It is well known that there is no absolute blood-brain barrier to antitoxin. Such experiments as we have cited, however, show the difficulty of bringing to the poisoned central neurons a sufficient amount of antitoxin quickly enough.

Our studies have led us to the belief that it is the toxin fixed within the central nervous system which is generally responsible for death. Undoubtedly the general metabolic disturbance and the attending loss of weight and strength and the fatigue may be contributing factors, and an occasional patient with tetanus may die without any convulsive manifestations at all, possibly from paralysis of the muscles of respiration. The experimental data indicate, however, that it is the toxin in the central nervous system which is ordinarily responsible for death.

TABLE II

THE THERAPEUTIC EFFECT OF TETANUS ANTITOXIN GIVEN INTRACISTERNALLY AND INTRAVENOUSLY IN GUINEA PIGS WITH GENERAL TETANUS*

| AMOUNT OF TETANUS ANTITOXIN IN AMERICAN UNITS | ROUTE OF ADMINISTRATION OF ANTITOXIN | | | |
|---|--------------------------------------|---------------------------------|-------------------|---------------------------------|
| | INTRACISTERNAL | | INTRAVENOUS | |
| | NO. OF ANIMALS | AVERAGE SURVIVAL IN DAYS† | NO. OF ANIMALS | AVERAGE SURVIVAL IN DAYS† |
| 70 | 2 | 4 | | |
| 140 | 2 | 4 | 2 | 3.7 |
| 210-280 | 4 | 3.3 | 4 | 3.7 |
| 350-500 | 6 | 4.7 | 6 | 3.8 |
| 560-700 | 4 | 4 | 6 | 4.3 |
| <i>Controls. No tetanus antitoxin.</i> | | | | |
| 0 | 9 | 2.8† | | |

*Each animal received 2 G-P LD50's of toxin intravenously. The T.A.T. was given 48 hours later, when all the animals had definite general tetanus (stiffness of body, erection of ears, etc.).

†All the animals died of tetanus.

Our problem then was to arrange an experiment in which we should have animals which were poisoned with more than a lethal dose of toxin, with undoubted signs of general tetanus, and with the certain fate of death from tetanus in the absence of treatment, and yet some of which at least would not have already fixed in their tissues a lethal dose of toxin, thus rendering them beyond any therapeutic aid. This experiment might have been possible with guinea pigs had we given a smaller and yet a lethal dose of toxin; had we given repeatedly smaller sublethal doses; or had we influenced the character of the disease by a preliminary injection of a quantity of antitoxin insufficient to protect from death but sufficient to induce a milder type of tetanus with a longer period of incubation. We felt, however, that it would be advisable for several reasons to shift our studies to dogs. Of chief importance was the fact that in guinea pigs we have found no demonstrable early infallible sign of general tetanus. By the time we are able to make a certain diagnosis, the animal has generalized rigidity of his voluntary musculature and in all likelihood already has fixed a lethal amount of toxin. In dogs, on the other hand, we have found that wrinkling or furrowing of the brows and erection of the ears in animals having received one or more lethal doses of toxin is an infallible sign of tetanus and that every such animal will become progressively sicker and will die if no treatment is instituted. We have here an early and unmistakable sign comparable to the early trismus in man which so commonly precedes general rigidity or convulsions. Furthermore, the ease and exactness with which antitoxin may be injected into the cisterna is greater in dogs than in guinea pigs.

Experiment 3 (Table III).—Forty-eight hours after the intramuscular injection of 2400 G-P LD50's of toxin per kilogram, all the dogs had

TABLE I

THE THERAPEUTIC EFFECT OF TETANUS ANTITOXIN GIVEN BY VARIOUS ROUTES, IN GUINEA PIGS WITH LOCAL TETANUS*

| AMOUNT OF TETANUS ANTITOXIN IN AMERICAN UNITS | ROUTE OF ADMINISTRATION OF ANTITOXIN | | | | | |
|--|--------------------------------------|-----------------------|---|-------------------|-----------------------|---|
| | INTRACISTERNAL | | | INTRAVENOUS | | |
| | NO. OF ANIMALS | NO. SURVIV- ING | AVERAGE SURVIVAL IN DAYS OF THOSE THAT DIED | NO. OF ANIMALS | NO. SURVIV- ING | AVERAGE SURVIVAL IN DAYS OF THOSE THAT DIED |
| <i>T. A. T. given 21 hr. after toxin. All animals had slight local stiffness.</i> | | | | | | |
| 1 | 1 | 0 | 7 | 1 | 0 | 6 |
| 2-7 | 4 | 4 | | 4 | 0 | 6.5 |
| 10-20 | 2 | 2 | | 3 | 1 | 12 |
| 25-154 | 8 | 8 | | 7 | 7 | |
| <i>T. A. T. given 23 hr. after toxin. All animals had slight local stiffness.†</i> | | | | | | |
| 0.1-0.8 | 4 | 0 | 5 | 4 | 0 | 4.5 |
| 1.2-2.0 | 2 | 1 | 8 | 3 | 0 | 5.7 |
| 3-7 | | | | 3 | 0 | 6 |
| 10-50 | 6 | 5 | 5‡ | 6 | 0 | 8 |
| 100 | 1 | 1 | | 1 | 1 | |
| <i>T. A. T. given 28 hr. after toxin. All animals had moderate local rigidity.</i> | | | | | | |
| 10-50 | 3 | 0 | 7 | 3 | 0 | 3 |
| 70-100 | 2 | 0 | 7 | 2 | 0 | 2.5 |
| 150-200 | | | | 2 | 0 | 2.5 |
| 300-400 | 2 | 0 | 3 | 2 | 0 | 3.5 |
| 500 | 1 | 0 | 8 | 1 | 0 | 6 |
| <i>Controls. No tetanus antitoxin.</i> | | | | | | |
| 0 | 17 | 0 | 3.3 | | | |

*Each animal received 2 G-P LD50's of toxin intramuscularly in a single dose in the thigh.

†Of 16 animals likewise treated with varying doses of tetanus antitoxin (0.1 to 100 A.U.) intramuscularly, none survived.

‡This animal kept head turned to left as if the brain stem had been traumatized at the time of injection. Autopsy showed no gross change.

injection of the toxin, none of the animals survived, although those which received antitoxin intracisternally lived longer than those which received it intravenously. This experiment demonstrated amply, we believe, the greater therapeutic efficacy of intracisternally over intravenously administered antitoxin in guinea pigs with local tetanus, all of which without treatment would have developed general tetanus shortly and died within forty-eight hours.

Experiment 2 (Table II).—We next attempted to evaluate this method of treatment in guinea pigs with general tetanus. Forty-eight hours after the intravenous injection of 2 G-P LD50's of toxin all the animals had unmistakable general tetanus. They were treated with varying doses of antitoxin intracisternally and intravenously. None survived, and there was little difference between the two groups. This failure, as well as the failure to save life in the third part of Experiment 1, is undoubtedly due to the fact that in these animals a lethal quantity of tetanus toxin had already been fixed and altered at the time treatment was begun.

TABLE IV

THE THERAPEUTIC EFFECT OF TETANUS ANTITOXIN GIVEN INTRACISTERNALLY AND INTRAVENOUSLY IN DOGS WITH LOCAL AND GENERAL TETANUS*

| AMOUNT OF TETANUS ANTITOXIN IN AMERICAN UNITS PER KG. | ROUTE OF ADMINISTRATION OF ANTITOXIN | |
|--|---|---------------------------|
| | INTRACISTERNAL | INTRAVENOUS |
| | RESULT | RESULT |
| 140 | Died of tetanus in 9 days; right lung consolidated | |
| 700 | Died with tetanus in 13 days following gavage and aspira- tion of vomitus; emaciation; ulceration of mouth | Died of tetanus in 6 days |
| 1400 | Died of tetanus in 14 days; emaciation; ulceration of mouth | Died of tetanus in 7 days |
| 2700 | Died of tetanus in 14 days; emaciation; ulceration of mouth | Died of tetanus in 8 days |

*Each dog received 1,200 G-P LD50's of toxin per kilogram intramuscularly. Seventy-two hours later they all had slight local stiffness and definite general tetanus.† At this time they received varying amounts of tetanus antitoxin by the routes indicated.

†Furrowing of brow, erection of ears, slight trismus, stiffness of neck and trunk, and slight or moderate stiffness of extremities.

NOTE: Autopsies negative except as otherwise stated.

used as controls. They died of tetanus in five and seven days. Of those in the next group with very early tetanus, the one treated by the cisternal route had only slight progression of symptoms and recovered. Of the three treated intravenously, two had slight progression of symptoms, one recovering and one dying of distemper in thirteen days; one became rapidly sicker and died of tetanus in six days. The next group had more advanced signs of early tetanus. The one which received antitoxin into the cisterna had no progression of symptoms and died later of distemper; whereas, one of those treated by intravenous injection showed some progression of symptoms but recovered, and the other became progressively more ill and was sacrificed moribund on the seventeenth day, having extreme tetanus, distemper, and an infected leg. In the next group with more advanced tetanus the one treated by the cisternal method recovered; whereas, the two treated by the intravenous route died of tetanus. The next group had beginning opisthotonos at the time of treatment. Five in which antitoxin was injected into the cisterna had no further progression of symptoms and recovered; whereas, the two having intravenous injection of antitoxin died with tetanus. The one animal with the most advanced tetanus at the time of treatment was given antitoxin intracisternally and died of tetanus in six days.

It will be seen that, if we disregard completely the important factor of the severity of the tetanus at the time of treatment, only 1 of 9 animals given antitoxin intracisternally died of tetanus; whereas, 6 of 9 given antitoxin intravenously succumbed, and all of the untreated

slight local and early general tetanus. They were given varying amounts of antitoxin by intracisternal or intravenous injection. The untreated controls died in from three to five days. The animals which had received 1 and 5 units of antitoxin per kilogram into the eisterna did not survive, although the latter lived three days longer than its mate which received the antitoxin into a vein. All those which received 25 units per kilogram or more in the eisterna lived. Their tetanus progressed rapidly on the day on which treatment was begun and they became so ill and so rigid that they lay prone and could not stand. Complete recovery followed. None of the dogs which received antitoxin intravenously survived.

TABLE III

THE THERAPEUTIC EFFECT OF TETANUS ANTITOXIN GIVEN INTRACISTERNAALLY AND INTRAVENOUSLY IN DOGS WITH LOCAL AND GENERAL TETANUS*

| AMOUNT OF TETANUS ANTITOXIN IN AMERICAN UNITS PER KG. | ROUTE OF ADMINISTRATION OF ANTITOXIN | |
|--|--------------------------------------|---------------------------|
| | INTRACISTERNAL | INTRAVENOUS |
| | RESULT | RESULT |
| 1 | Died of tetanus in 6 days | Died of tetanus in 7 days |
| 5 | Died of tetanus in 9 days | Died of tetanus in 6 days |
| 25 | Severe general tetanus | Died of tetanus in 4 days |
| | Complete recovery | |
| 125 | Severe general tetanus | Died of tetanus in 8 days |
| | Complete recovery | |
| 625 | Severe general tetanus | Died of tetanus in 9 days |
| | Complete recovery | |
| <i>Controls. No tetanus antitoxin.</i> | | |
| 0 | Died of tetanus in 3 days | |
| 0 | Died of tetanus in 4 days | |
| 0 | Died of tetanus in 5 days | |

*Each dog received 2,400 G-P LD50's of toxin per kilogram intramuscularly. Forty-eight hours later they all had slight local and early general tetanus.† At this time they received varying amounts of antitoxin by the route indicated. Three hours after injection of tetanus antitoxin they all had well-marked general tetanus.

†Wrinkling of brows, erection of ears, stiffness of neck.

NOTE: Autopsies were negative on all of the animals.

Experiment 4 (Table IV).—Nine dogs were given 1200 G-P LD50's of toxin per kilogram intramuscularly. Seventy-two hours later all had slight local stiffness and fairly advanced general tetanus. They were treated at this time. None survived. Those treated by intracisternal injection, however, lived consistently longer than those treated by intravenous injection.

Experiment 5 (Table V).—Twenty-one dogs received 600 G-P LD50's of toxin per kilogram intravenously. Forty-nine hours later they were classified according to severity of symptoms and were treated with 750 American units of antitoxin per kilogram. One animal had no symptoms at this time and was kept as a control. He became prone and had convulsions on the fifth day and died in three weeks. Two other animals with only questionable early symptoms at this time were likewise

controls died. Likewise, it is evident that among those which survived there was less progression of the disease in the animals treated intracisternally.

In this, as in all the other experiments, where any disparity in the signs of tetanus existed at the time of treatment, the animals with the severer signs of tetanus were treated with injection of antitoxin into the cisterna in order to put this mode of treatment to the severer test. In all instances where we have stated the outcome as "died of tetanus" the tetanus had become progressively worse and was so extreme at the time of death that, from our experience, we felt that the dog could not recover regardless of the presence or absence of complications. On the other hand, when an animal is said to have "died of distemper" or from some other cause, the tetanus had been steadily improving before death and it appeared evident that complete recovery would have taken place in the absence of complications. After the single injection of antitoxin all animals were treated exactly alike. Before and after this treatment they were fed the regular laboratory diet of biscuits supplemented with milk and raw ground meat. As soon as they became prone, all were given either daily gavage of sweetened milk or, more commonly, intravenous infusions of normal salt solution and 5 per cent glucose, generally two a day of 100 c.c. each. They were turned frequently. In spite of our efforts most of those lying prone with convulsions for a long time lost weight. Frequently their lips became somewhat ulcerated. Autopsies were done on all. Both intravenous and intracisternal injections were made in unanesthetized animals.

Experiment 6 (Table VI).—This experiment confirms the preceding one. Twenty dogs were given 840 G-P LD50's of toxin intravenously per kilogram. Fifty-two hours later they were grouped according to symptoms and treated with 750 units of antitoxin per kilogram. The one with the mildest symptoms was kept as a control. He died in seven days. In the next group 4 received antitoxin into the cisterna. One died within thirty hours, obviously not of tetanus, and at autopsy showed a hemorrhage in the medulla from inadvertent penetration of the needle during the attempted intracisternal injection and should properly be excluded from the experiment. One in which the tetanus had advanced slightly and then improved steadily, died of distemper. One had no progression of symptoms; one, slight progression. Both recovered. Four treated by intravenous injection exhibited some progression of the tetanus, but 2 recovered, 1 died of distemper, and only 1 died of tetanus. The 2 controls died of tetanus. In the next group 4 received antitoxin by the intracisternal route. The tetanus advanced slightly in 3; 2 recovered, and 1 died of distemper. One became so ill it lay prone with convulsions but recovered completely. Of the 3 treated by the intravenous route, 2 succumbed to tetanus, and 1, which lay prone with convulsions for nearly 2 weeks, eventually recovered. In the last group the dog treated with intracisternal injection of antitoxin developed advanced tetanus but recovered; whereas, its mate treated with intravenous injection died of tetanus.

As in the preceding experiment, if we ignore the degree of tetanus at the time of treatment, none of those given antitoxin into the cisterna

TABLE V

THE THERAPEUTIC EFFECT OF TETANUS ANTITOXIN GIVEN INTRACISTERNALLY AND INTRAVENOUSLY IN DOGS WITH GENERAL TETANUS*

| SYMPTOMS AT TIME OF TREATMENT | ROUTE OF ADMINISTRATION OF ANTITOXIN | | |
|--|--|--|---|
| | INTRACISTERNAL | INTRAVENOUS | CONTROLS—NO TETANUS ANTITOXIN |
| | RESULT | RESULT | RESULT |
| None | | | D & J† in 5 days; died of tetanus in 21 days; emaciation |
| Questionable furrowing of brows and erection of ears | | | D & J in 4 days; died of tetanus in 5 days Body stiff in 4 days; died of tetanus in 7 days |
| Slight furrowing of brows and erection of ears | Body slightly stiff in 3 days; recovery | Body stiff in 4 days; no further progression; died of distemper in 13 days; pneumonia Body slightly stiff in 4 days; recovery D & J in 5 days; died of tetanus in 6 days | |
| Erection of ears, furrowing of brows, slight stiffness of neck | No progression of symptoms, died of distemper in 10 days; pneumonia | Neck became more rigid; no further progression; recovery D & J in 5 days; moribund in 17 days; sacrificed; extreme tetanus, distemper, ulcer face, infected leg | |
| Rather marked stiffness of neck, ears erect, brows furrowed | Body slightly stiff in 3 days; recovery | D & J in 7 days; died of tetanus in 14 days; had distemper; slight consolidation of lung D & J in 5 days; died of tetanus in 18 days | |
| Ears erect, brows furrowed, body stiff; beginning opisthotonos | No progression; recovery No progression; recovery No progression; recovery No progression; recovery | D & J in 7 days; died of tetanus in 15 days; had distemper. D & J in 7 days; died of tetanus in 8 days | |
| Marked stiffness of body | D & J in 4 days; died of tetanus in 6 days | | |

*Each dog received 600 G-P LD50's of toxin intravenously per kilogram. Forty-nine hours later they were divided into two groups according to symptoms and treated with tetanus antitoxin as indicated. Each received 750 American units per kilogram.

†D & J signifies that the animal was prone, unable to stand, and jerking almost constantly in clonic convulsive movements. Autopsies were negative except where otherwise indicated.

controls died. Likewise, it is evident that among those which survived there was less progression of the disease in the animals treated intracisternally.

In this, as in all the other experiments, where any disparity in the signs of tetanus existed at the time of treatment, the animals with the severer signs of tetanus were treated with injection of antitoxin into the cisterna in order to put this mode of treatment to the severer test. In all instances where we have stated the outcome as "died of tetanus" the tetanus had become progressively worse and was so extreme at the time of death that, from our experience, we felt that the dog could not recover regardless of the presence or absence of complications. On the other hand, when an animal is said to have "died of distemper" or from some other cause, the tetanus had been steadily improving before death and it appeared evident that complete recovery would have taken place in the absence of complications. After the single injection of antitoxin all animals were treated exactly alike. Before and after this treatment they were fed the regular laboratory diet of biscuits supplemented with milk and raw ground meat. As soon as they became prone, all were given either daily gavage of sweetened milk or, more commonly, intravenous infusions of normal salt solution and 5 per cent glucose, generally two a day of 100 c.c. each. They were turned frequently. In spite of our efforts most of those lying prone with convulsions for a long time lost weight. Frequently their lips became somewhat ulcerated. Autopsies were done on all. Both intravenous and intracisternal injections were made in unanesthetized animals.

Experiment 6 (Table VI).—This experiment confirms the preceding one. Twenty dogs were given 840 G-P LD50's of toxin intravenously per kilogram. Fifty-two hours later they were grouped according to symptoms and treated with 750 units of antitoxin per kilogram. The one with the mildest symptoms was kept as a control. He died in seven days. In the next group 4 received antitoxin into the cisterna. One died within thirty hours, obviously not of tetanus, and at autopsy showed a hemorrhage in the medulla from inadvertent penetration of the needle during the attempted intracisternal injection and should properly be excluded from the experiment. One in which the tetanus had advanced slightly and then improved steadily, died of distemper. One had no progression of symptoms; one, slight progression. Both recovered. Four treated by intravenous injection exhibited some progression of the tetanus, but 2 recovered, 1 died of distemper, and only 1 died of tetanus. The 2 controls died of tetanus. In the next group 4 received antitoxin by the intracisternal route. The tetanus advanced slightly in 3; 2 recovered, and 1 died of distemper. One became so ill it lay prone with convulsions but recovered completely. Of the 3 treated by the intravenous route, 2 succumbed to tetanus, and 1, which lay prone with convulsions for nearly 2 weeks, eventually recovered. In the last group the dog treated with intracisternal injection of antitoxin developed advanced tetanus but recovered; whereas, its mate treated with intravenous injection died of tetanus.

As in the preceding experiment, if we ignore the degree of tetanus at the time of treatment, none of those given antitoxin into the cisterna

TABLE VI

THE THERAPEUTIC EFFECT OF TETANUS ANTITOXIN GIVEN INTRACISTERNALLY AND INTRAVENOUSLY IN DOGS WITH GENERAL TETANUS*

| SYMPTOMS AT TIME OF TREATMENT | ROUTE OF ADMINISTRATION OF ANTITOXIN | | |
|--|---|--|---|
| | INTRACISTERNAL | INTRAVENOUS | CONTROLS—NO TETANUS ANTITOXIN |
| | RESULT | RESULT | RESULT |
| Beginning erection of ears, furrowing of brows | | | Body stiff in 4 days; died of tetanus in 7 days |
| Ears erect, brows furrowed | No progression; recovery Body stiff in 4 days; better in 8 days; recovery Body stiff in 4 days; improvement; died of distemper in 10 days; pneumonia; empyema Body slightly stiff in 3 days; dead next A.M.; hemorrhagic tract in medulla from needle trauma | Body stiff in 4 days; recovery Body stiff in 4 days; recovery Body stiff in 4 days; prone in 8 days; died of tetanus in 9 days; slight consolidation one lobe Body stiff in 4 days; died of tetanus in 6 days | D & J† in 5 days; died of tetanus in 5 days D & J in 4 days; died of tetanus in 5 days |
| Ears erect, brows furrowed, body moderately stiff | Body stiff in 4 days; better in 6 days; recovery Body stiff and distemper in 4 days; no progression of tetanus; died of distemper in 9 days; pneumonia; empyema Body stiff in 4 days; recovery D & J in 7 days; up next day; recovery | D & J in 6 days; prone 2 weeks, recovery D & J in 4 days; died of tetanus in 16 days D & J in 4 days; died of tetanus in 18 days | |
| Ears erect, brows furrowed, body rather markedly rigid | D & J in 6 days, up next day, recovery | D & J in 3 days; died of tetanus in 5 days | |

*Each dog received 840 G-P LD50's of toxin intravenously per kilogram. Fifty-two hours later they were divided into groups according to symptoms and treated with tetanus antitoxin as indicated. Each received 750 American units per kilogram.

†D & J signifies that the animal was prone, unable to stand, and jerking almost constantly in clonic convulsive movements. Autopsies were negative except where otherwise indicated.

died of tetanus; whereas, 5 of 8 receiving antitoxin intravenously did die of tetanus.

DISCUSSION

These experiments offer evidence that tetanus antitoxin given intrathecally is much more efficacious as a therapeutic agent in animals which have received more than a lethal dose of tetanus toxin and which have

local or general tetanus than tetanus antitoxin given intravenously. The reason for this is not entirely clear. Ransom²⁴ claims to have demonstrated that most of the antitoxin introduced intrathecally passes fairly rapidly into the blood stream, although Blumenthal and Jacob²⁵ state that antitoxin given by subdural infusion remains for at least twenty hours in the cerebrospinal fluid of goats. According to our knowledge of the absorption of cerebrospinal fluid, this is what one should expect. But does some of the antitoxin, perhaps only a small fraction of it, pass directly into the central nervous system? We know that when we inject pontocaine or novocain or some other local anesthetic agent into the subarachnoid space, most of it penetrates directly through the pia and into the substance of the cord, for there follows an anesthetic effect roughly localized to that area of cord with which the solution comes in contact. It may be possible that some of the antitoxin similarly diffuses into the substance of the cord or brain stem. It is true that the molecule of tetanus antitoxin is in all likelihood larger than that of these anesthetic agents. And yet we know that the antitoxin molecule is not too large to pass through the capillary walls of blood and lymph vessels into the various body tissue spaces and vice versa. Until some other explanation is at hand we shall have to assume that it can similarly pass from the cerebrospinal fluid into the substance of the central nervous system.

We have previously pointed out that antitoxin injected directly into the medulla is at least a thousand times more efficacious against toxin previously placed there than is antitoxin injected intravenously. If we can assume then that some of the antitoxin injected into the cerebrospinal fluid, even a small part of it, passes directly into the central nervous system, we can readily understand its greater therapeutic efficacy.

Our experiments do not constitute the first attempt to evaluate the therapeutic effect of intrathecal injections of antitoxin. In 1898 Sicard²⁶ found that injections of large amounts of antitoxin into the lumbar subarachnoid space of dogs at the onset of symptoms of tetanus would stop the advance of symptoms and save life; whereas, the subcutaneous injection of the same amount was inefficacious. In the same year Blumenthal and Jacob²⁵ reported that "dural infusion" of antitoxin in goats at the onset of symptoms following the intramuscular injection of several lethal doses of toxin was without effect. In 1914 Permin²⁷ reported no difference in goats with trismus between the intravenous and intrathecal routes.

On the other hand, Park and Nicoll²⁸ described at the same time some experiments on guinea pigs which they felt "would seem absolutely conclusive of the superiority of the intraspinal over the intravenous method." Their animals were treated with varying amounts of antitoxin eighteen to twenty-three hours after the intramuscular injection

of 2 M. L. D. of toxin. Their results are similar to those we have reported in Table II. Their intrathecal injections were made in the lumbar space after incision down to the dura, the intravenous injections into the heart. They demonstrated that when the same amount of antitoxin was given it was more efficacious in saving life if given intrathecally than either intravenously or intraneurally and that a smaller dose was efficacious if injected intrathecally rather than by these other routes.

Gottlieb and Freund²⁹ also found in 1916 that rabbits having received 3 M.L.D. of toxin intramuscularly could not be saved with 1 c.c. of antitoxin given intravenously, even 6 hours after injection; whereas, they could be protected with the same amount of antitoxin given intracisternally up to 25 hours after injection of the toxin.

In 1917 Sherrington's much cited experiments with monkeys were reported.³⁰ His results may be summarized as follows: All were given approximately 8 lethal doses of toxin intramuscularly. The controls had local tetanus in about 30 to 36 hours, general tetanus by the end of the third day, and died on the fourth or fifth day. Each treated animal received 2,000 American units of antitoxin per kilogram 47 to 78 hours after injection of the toxin. Twenty-five were treated by subcutaneous injection and only 2 survived (tetanus antitoxin 50 and 70 hours after injection); 25 were treated by intramuscular injection with 3 survivals (tetanus antitoxin 47, 50, and 52 hours after injection); 25 were treated intravenously with 7 survivals (tetanus antitoxin 57, 50, 50, 51, 51, 54, and 70 hours after injection); 10 were treated with antitoxin injected under the cerebral dura without any survivals. In contrast to these results, of 25 treated with antitoxin in the lumbar subarachnoid space, 13 survived (tetanus antitoxin 47, 48, 50, 50, 51, 51, 51, 52, 52, 53, 54, 66, 68, and 70 hours after injection) and of 20 treated by the bulbar intrathecal route 13 survived (tetanus antitoxin 47, 48, 50, 51, 52, 53, 56, 66, 66, 68, 70, and 70 hours after injection).

Finally, Florey and Fildes³¹ presented some work on rabbits which they felt showed no advantage in the cisternal route. They gave 4 M.L.D. of toxin intramuscularly, a dose found to cause local tetanus in 24 hours and death on the third day. They treated ten rabbits on the second day by operative exposure and injection into the cisterna of 1,000 units of antitoxin and gave simultaneously 15 c.c. of hypertonic salt solution intravenously. They concluded that, when local tetanus was confined to stiffness of the injected leg, all survived, whether treated intravenously or intracisternally, but that when there was the slightest involvement of the head (general tetanus) all died.

It is likely that the good results reported by Roux and Borrel²⁰ and von Török³² with antitoxin injected into the cerebrum (a method of administration which obviously cannot be considered in man) are to

be explained on the basis that a large part of the injected antitoxin passes into the ventricular and subarachnoid fluids. Roux and Borrel state that without doubt the injected antitoxin penetrates into the ventricle. Schaeffer and Muckenfuss,³³ using India ink in monkeys, found that the material when injected into the cerebrum reaches the ventricles and subarachnoid space if more than 0.5 c.c. of fluid is injected. Friedmann, Zuger, and Hollander³⁴ likewise found that dyes injected into the cerebrum passed in large part into the lateral ventricles. Similarly, the occasional good results which have been reported with injection of antitoxin into the sciatic nerve near the sciatic foramen may possibly be due to the forcible injection of antitoxin through the nerve and into the subarachnoid space. For an analysis of the explanation of passage of fluid along nerves into the cerebrospinal fluid, not by any natural pathway, but by forceful driving of the fluid with pressure, see the comments of Abel and his co-workers.³

We see, therefore, that most workers have found the intrathecal route to be superior. The failures are, we believe, easy to understand. From our own work it is apparent that, if animals are treated early enough with a sufficient dose of antitoxin, all will survive whether treated by the intrathecal or the intravenous method; and that, conversely, if the treatment is delayed so long that a fatal amount of toxin has been already fixed, antitoxin given by either route will be futile. Furthermore, if one treats animals in between these two periods, that is to say, if they have more advanced symptoms than in the first instance and yet have not undergone fixation of a lethal dose as in the second, success or failure in finding the intracisternal route superior will depend upon varying the dose or upon selecting a proper single dose. Too small a dose may fail to demonstrate a difference between the intrathecal and intravenous routes, as in the animals receiving the smallest doses in the first and second parts of Experiment 1 or in the first pair of dogs in Experiment 3.*

The criticisms which have been made of the experimental demonstration of the superiority of intrathecal injection of antitoxin are well summarized in Huntington's evaluation of Sherrington's work.¹⁵ In the first place, Huntington points out that tetanus toxin and not actual infection with the *Clostridium tetani* was employed. In answer to this criticism it may be pointed out that the pathogenic effect of tetanus infection is manifested only by the toxin and not by the organism per se. The use of tetanus toxin is simply a convenient method of producing tetanus of a measurable degree. In the second place, he points to the enormous dosage of antitoxin which Sherrington used. In other experiments smaller doses have been utilized. In our own experiments with dogs, for example, the 750 units per kilogram used would amount

*The superiority of the intrathecal method was not apparent in our earlier studies and accounts for the incorrect statement made by one of us.²

to only 48,750 units in a 65 kilogram man if a comparable amount were given. One would be willing to employ very large amounts of antitoxin if this procedure held any promise of therapeutic benefit. In the third place, Huntington states that man is "vastly" more susceptible to tetanus than is the monkey. As a matter of fact, the consensus is that man is of the same order of sensitivity as the guinea pig and the monkey. It is observed that comparable results with intrathecal injection of antitoxin have been obtained on animals of such diverse sensitivity as the very sensitive guinea pig and monkey and the relatively resistant dog. We have been interested in the behavior of animals of varying sensitivity or resistance to tetanus and conclude that, although different species succumb to widely different amounts of toxin, they all behave similarly as far as their fundamental reaction to tetanus toxin is concerned. Furthermore, we feel that there are only quantitative, not fundamental, differences in the action of tetanus antitoxin on tetanus toxin in the body of both tetanus-sensitive and tetanus-resistant species. Finally, Huntington feels that it is unfair to transfer results from animals suffering from local tetanus alone to man suffering from general tetanus. Our own experiments demonstrate that the same superiority of intrathecal injection of antitoxin holds true with general as well as with local tetanus. It is our feeling that tetanus antitoxin given in proper amount intrathecally will be found superior to antitoxin administered intravenously in any animal poisoned with a lethal quantity of tetanus toxin, with evident symptoms of tetanus, and yet before a fatal amount of toxin has been fixed. We feel that this will hold true for any animal, tetanus-sensitive or tetanus-resistant, including man. We also feel that it will hold true whether the toxin is injected into the body or liberated from tetanus organisms in the body tissue.

For obvious reasons we have purposely omitted reference to clinical reports concerning the relative efficacy of antitoxin given by various routes. With clinical material there is no way of estimating the exact severity of the disease in each instance. The severity of the disease and the prognosis are known to vary with the length of the incubation period, the duration of the disease at the time treatment is begun, the initial symptoms, and other factors. Even if all these data were available in the published reports, and they are not, it would still be difficult to be certain that a group of patients treated in one manner had tetanus of comparable severity with that of a group treated in a different manner. It is a common observation that the mortality from tetanus in any one hospital may vary widely from one period to another, even though the same treatment is used. Furthermore, some of the clinical studies are reported in the literature because the particular treatment employed seemed to have given unusually good results; whereas, reports of other patients treated in the same manner are never published because the outcome has not been so favorable. It appears that the merits

of treatment by intrathecal injection can better be investigated by carefully controlled experimental studies. It is true, of course, that a number of clinicians have differed from the majority all along and have felt that the intrathecal route should be used and that it gives more satisfactory results than do the other methods.

Certain problems remain to be solved. Especially is it important to ascertain whether repeated intrathecal injections are more beneficial than a single one and whether the lumbar subarachnoid route is as efficacious as the cisternal. This work is being pursued. There remains to find out the proper dosage, the number of injections, and the intervals between them which are best suited to the treatment of tetanus.

CONCLUSIONS

1. Experiments are reported which demonstrate that tetanus antitoxin administered intrathecally is superior to that given intravenously in guinea pigs having received more than a lethal dose of tetanus toxin and exhibiting local tetanus, and in dogs poisoned with more than a lethal dose of toxin and showing signs of both local and general tetanus.

2. The significance of these and related experiments is discussed. An explanation of the failure of other workers to demonstrate the superiority of antitoxin administered by intrathecal injection is given.

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THE PANCREATICOHEPATIC SYNDROME

PANCREATIC FIBROSIS AND FATTY LIVER

WARREN H. COLE, M.D., AND J. S. HOWE, M.D., CHICAGO, ILL.

(From the Departments of Surgery and Pathology, University of Illinois College of Medicine)

WHEN Fisher¹ and Allan and associates² (1924) discovered that pancreatectomy in the dog led to fatty infiltration of the liver and death of the animal in two to eight months, they laid the foundation for the recognition of a human clinical syndrome consisting primarily of an atrophy or sclerosis of the pancreas with fatty infiltration of the liver. Insulin, of course, was given to the animals to prevent diabetes. Allan and his co-workers noted that insulin removed the fat in the liver which might be deposited within a few days following the pancreatectomy but that the fatty infiltration would recur weeks later. These same authors also noted that the addition of raw pancreas to the diet of these dogs would prevent the deposition of fat in the liver. A few years later Hershey and Soskin³ noted that the addition of lecithin (as obtained from egg yolk) to the diet of pancreatectomized dogs would also prevent death from fatty infiltration of the liver. A year or two later Best, Ferguson, and Hershey⁴ showed that the action of lecithin in the prevention of fatty liver was most likely due to the choline contained in it.

Perhaps the most important contribution to the phenomenon of fatty liver in pancreatic insufficiency was made by Dragstedt and associates⁵ in 1936. They made an alcoholic extract of beef pancreas which, when given to pancreatectomized dogs, would prevent the fatty liver. They have called this substance lipocaic. Best and Ridout⁶ tried lipocaic preparations made after the method of Dragstedt and associates and concluded that the effectiveness was perhaps due to the choline and other unknown factors in the proteins contained in the lipocaic extract, although they admit that the "extract contains only small quantities of choline." In a recent article Dragstedt⁷ appears to have demonstrated satisfactorily that the effectiveness of lipocaic is not due to the choline contained in it. Dragstedt states that "it requires approximately 2 grams of choline a day over and above that present in the diet to exert this beneficial effect, whereas 100 grams of pancreas, which is an effective dose, contains only about 250 mg. of choline." He notes also that "liver and brain which contain as much or more lecithin and choline, exert no beneficial effect."

The next problem in the study of the mechanism of production of fatty liver by pancreatectomy lies in the question of whether the action is due to the loss of the internal or external secretion. Elman and McCaughan⁸ and others have called attention to the importance of the ex-

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TABLE I

| CONGENITAL PANCREATIC STEATORRHEA | CELIAC DISEASE |
|--|---|
| Symptoms since birth | Onset 9 months to 2 years |
| Oil present in stool | Oil not present in stool |
| High fecal fat; large amount unsplit | High fecal fat; well split |
| Glucose tolerance curve on high side of normal | Glucose tolerance curve flat |
| Post mortem shows lesion in pancreas | Post mortem shows no lesion in pancreas |

However, it should be stated that there is not a complete agreement (Hess and Saphir¹⁴) as to the definition of the term celiac disease, particularly as to the absence of a pathologic lesion in the pancreas. With the exception of the points mentioned above, the symptoms and physical findings of pancreatic steatorrhea are identical to those in non-pancreatic steatorrhea (celiac disease). The chief differences therefore lie in the pathologic findings in the pancreas and the type of fat in the stool; i.e., the amount of neutral fat and fatty acids. The numerous points of similarity suggest therefore that the two diseases may be the same except that celiac disease is an earlier stage or is an expression of the results of pancreatic dysfunction in the absence of demonstrable pathologic changes in the organ.

Another disease with evidence of pancreatic dysfunction as evidenced by fatty diarrheal stools is sprue. Writers on the subject have been inclined to divide the disease into two divisions, tropical and nontropical sprue; but in a recent study Snell¹⁵ finally concludes that the two diseases are the same. He remarks that nontropical sprue may represent a more advanced stage of the disease largely through delay in diagnosis. However, since pancreatic lesions are absent in each group and pancreatic enzymes are found in the duodenum, it appears likely that sprue and the pancreaticohepatic syndrome (pancreatic steatorrhea) are not identical. However, the manifestations of sprue including glossitis, stomatitis, anemia, fatty diarrhea, emaciation, low blood calcium, low blood protein, osteoporosis, low blood cholesterol, etc., are remarkably similar to those found in pancreatic steatorrhea. The great difference lies in the fact that in sprue anemia is more pronounced and is relieved by liver therapy. Sprue therefore might be considered an intermediary disease between pernicious anemia and pancreatic steatorrhea.

ETIOLOGY

After reviewing the cases of fatty infiltration of the liver secondary to pancreatic dysfunction (with pathologic confirmation in the pancreas), it appears that the disease described in childhood as pancreatic steatorrhea and the disease more recently described in adults with fatty liver and pancreatic sclerosis are the same. However, the etiologic factor and pathogenesis of the pancreatic disease may be slightly different. In childhood Andersen¹¹ has suggested three possible etiologic factors for the pancreatic fibrosis: (1) congenital malforma-

ternal secretion of the pancreas to the well-being of the animal. Berg and Zucker⁹ obtained fatty changes in the liver of dogs which survived eighty days or longer following diversion of the external secretions to the outside. However, Dragstedt and associates¹⁰ could not duplicate the findings and concluded that neither loss of external secretion by pancreatic fistula nor ligation of all the pancreatic ducts would result in the type of fatty liver as noted following pancreatectomy. In a more recent publication Dragstedt⁷ implies that the factor preventing the fatty liver must be a second component of internal secretion, particularly since feeding of pancreatic juice does not prevent the fatty infiltration, even though it does improve the digestion and absorption of food.

RELATIONSHIP OF PANCREATICOHEPATIC SYNDROME TO OTHER DISEASES

Up to the present time there are relatively few of the "typical" type of fatty liver and pancreatic atrophy reported in adults (six, including the one herein described). However, there are several allied diseases which bear a direct resemblance to the syndrome. Perhaps the condition bearing the most resemblance is childhood pancreatic steatorrhea which has had the terms cystic fibrosis of the pancreas, congenital steatorrhea, etc., applied by various authors. It is our opinion that this disease is identical to the one under discussion in this report, with one notable exception; namely, that it occurs in childhood, whereas the other group occurs in adults.

Andersen¹¹ has recently made a study of forty-nine cases (as collected from various sources) of fibrosis of the pancreas in infants and children. She noted that in nineteen instances fatty infiltration of the liver existed. Of more importance was the fact that 60 per cent of the patients in the older group, i.e., from 6 months to 14½ years of age, had fatty infiltration of the liver. In animals we know that it takes several weeks or months for pancreatic deficiency to produce a fatty liver and that in human beings it presumably takes even longer. It is therefore obvious that the absence of a fatty liver in an infant only a few months old does not exclude the disease. Clinical manifestations as noted by Andersen and others include malnutrition, frequent bulky foul stools after the age of 6 months, protuberant abdomen, anemia, muscular weakness, and mild osteoporosis, all of which are manifestations similar to those described in celiac disease. Not all instances of fibrosis of the pancreas have the bulky, fatty, foul-smelling stool even though the process has advanced to the stage where fatty infiltration of the liver is advanced. This is illustrated by a case (patient aged 4 years) reported by Davie.¹² Bronchiectasis and pneumonia are common in pancreatic steatorrhea of childhood; death is almost always secondary to or accompanied by the latter.

In spite of the similarity of congenital pancreatic steatorrhea to celiac disease, there are a few points of dissimilarity. These have been summarized by Harper¹³ as follows (Table I):

process which may obstruct the ducts. There appear to be enough clinical data to support this assumption, in spite of the fact that simple ligation of the ducts in dogs will not produce a typical fatty liver. The difference may be in the fact that in operative ligation of ducts there is no accompanying infection; whereas, in human beings the process producing the obstruction (even if stones) is apt to be accompanied by infection. Another important feature may lie in anatomical variations, so far as obstruction of the duct of Wirsung would obviously be most damaging in the instances when the accessory duct was poorly developed or not anastomosing with the duct of Wirsung. In the average pancreas (human and dog) there is a certain amount of anastomosis between the two duct systems.

CLINICAL MANIFESTATIONS

A study of the five adult cases previously reported by various authors and the one herein discussed reveals the fact that the manifestations are extremely variable. The duration of symptoms likewise varies from eight months to twenty years, depending upon the cause. Conforming to the definition of the disease requiring pancreatic fibrosis and fatty infiltration of the liver as prerequisites, the manifestations will consist largely of symptoms produced by lesions of these organs. However, it is a notorious fact that symptoms produced by diseases of these two organs are insidious and extremely varied. The fact that other organs are likely to be affected in a functional way in the absence of pathologic lesions is bound to add to the inconsistencies in the manifestations. The disease attacks males equally as often as females; in adults it may be encountered in any decade.

One of the earliest manifestations is the passage of frequent, foul, fatty, bulky stools. However, in two of the six adult cases available for study, stool changes were insignificant. One of the most common complaints is weakness. Loss of weight may occur, but two of the six cases were obese. Anorexia, nausea, and vomiting are frequent and may occur in attacks with or without abdominal pain. Mild pain and discomfort in the epigastrium related presumably to the pathologic changes in the liver and pancreas are common. When the pancreatic lesion is secondary to gall bladder disease, there may naturally be attacks of severe pain located particularly in the right upper quadrant.

Obviously the size of the liver will depend upon the amount of fat contained in it. In the case herein reported the liver extended down about 6 cm. Various tests of hepatic function, including the hippuric acid and bromsulphalein tests, have been positive; as would be expected, the blood protein may likewise be lowered (Table II).

Cardiac manifestations, including dyspnea, etc., have been noted at times and in the case herein reported were substantiated by severe fatty changes in the myocardium (see autopsy protocol, case report). Hypertension has been noted on only one occasion and is perhaps coincidental.

tion of the ducts, (2) inflammation of the pancreas in fetal life, and (3) vitamin A deficiency. In adults it likewise appears that several factors are possible.

Although there have been cases reported with post-mortem findings in which pancreatic disease and fatty liver were noted along with other findings (Choy and Oh,¹⁶ Paviot and associates,¹⁷ and others), Snell and Comfort¹⁸ were perhaps the first to emphasize the importance of the pancreatic lesion in the production of the fatty liver, particularly as a corollary to the production of fatty infiltration of the liver to pancreatectomy in dogs.

Up to the present time there are reports of six cases in the literature, including the one herein discussed. Three were reported by Snell and Comfort. In the case herein reported it appears that gall bladder disease was perhaps the primary cause of the severe fibrosis and atrophy of the pancreas, aided perhaps by an old penetrating duodenal ulcer. The presence of gall bladder disease (with stones) in Rosenberg's¹⁹ case, along with a possible cholecystitis in two of the other four cases, suggests that gall bladder disease may be an important etiologic factor. The importance of this possible relationship becomes more apparent when we recall that the gall bladder is diseased (usually with stones) in such a large percentage of patients with acute pancreatitis and is probably the direct etiologic factor in the development of the pancreatitis. In two of Snell's patients pancreatic lithiasis appears to have been the cause of the pancreatic fibrosis with insufficiency, but the cause of the pancreatic stones is, of course, obscure. In the case reported by Norris, Beard, and Gerber,²⁰ a small carcinoma was found in the head of the pancreas. Whether or not this could have been responsible for the severe grade of pancreatic atrophy is not certain. Even if it is assumed that the tumor was compressing the duct of Wirsung, would this be sufficient to cause atrophy and fibrosis because of obstruction of the duct over such a short time? It appears doubtful.

It becomes obvious then that more cases will have to be studied before any conclusion may be reached as to the predominating etiologic factor causing the pancreatic lesion. The recent experiments of Chaikoff²¹ suggest that vitamin deficiency may be an important factor in the development of the disease so far as he has been able to keep two dogs alive for at least four years after pancreatectomy when they were fed vitamins A, B, and D along with lean meat, sucrose, and bone ash. In children Andersen¹¹ has suggested that vitamin A deficiency may be an important factor in the etiology. The other two possible factors suggested by Andersen were congenital malformation (duct obstruction) and fetal acute pancreatitis.

It, therefore, appears safe to assume that the fatty infiltration of the liver is always secondary to a severe pancreatic insufficiency incident to pancreatic atrophy and fibrosis. Undoubtedly, the pancreatic fibrosis may be caused by numerous factors as described above, including any

Although two of the six cases studied were obese, this feature may also be coincidental; both of these cases had hirsutism. Ascites and edema of the extremities have been noted too often to be of only coincidental significance. Since renal damage has been insignificant in all cases studied, the causative factors of the ascites would appear to be the heart and liver. Only two of the six cases had diabetes. In view of the fact that pancreatic destruction may be so pronounced, one might expect diabetes to be observed more commonly. However, when we consider that the glycosuria or diabetes accompanying the destructive types of acute pancreatitis is mild and commonly absent, the infrequency of diabetes in pancreaticehepatic disease is not inconsistent. Apparently the viability of relatively few islands of Langerhans is sufficient to prevent diabetes.

Laboratory tests, in addition to the liver function tests and urine examination previously mentioned, may be helpful. Snell and Comfort¹⁸ call attention to the absence or diminution of pancreatic enzymes in the duodenal secretion. On two occasions there has been no free hydrochloric acid in the stomach. This finding may be of considerable significance because gastric analysis was not performed on all the cases studied. Anemia appears to be a fairly constant finding, being observed in four of six cases. The serum amylase in our case was very low before operation, but was elevated above normal after operation. The low reading was presumably an expression of hepatic insufficiency; Somogyi²² has called attention to this relationship, a finding which we have been able to corroborate. The blood cholesterol is usually lower than normal. As stated, there seems to be a definite tendency toward a lowering of the blood protein level, with a shift toward reversal of the albumin-globulin ratio. According to the experience of Keeton and his associates²³ and others, this would be corroborative evidence toward the existence of hepatic insufficiency.

A study of the manifestations encountered in the so-called pancreaticehepatic syndrome shows a definite similarity to those described years ago (1923) by Whipple²⁴ as pancreatic asthenia. However, he was describing an acute condition observed as a postoperative complication. For example, the anorexia, nausea, vomiting, apathy, and loss of weight are symptoms in common. In his group he noted a lowering of blood pressure and occasionally a tendency toward hemorrhage. Glycosuria was not significant.

The symptoms of pancreatic steatorrhea of infancy and childhood, as noted previously, consisting primarily of steatorrhea, diarrhea, loss of weight, anemia, protuberant abdomen, mild osteoporosis, and tendency to bronchiectasis and pneumonia, are remarkably similar to the symptoms herein discussed as belonging to the pancreaticehepatic syndrome. Points of difference consisting, for example, of mild osteoporosis would be readily explained because of growth requirements in children.

TABLE II
SUMMARY OF CASES REPORTED AS PANCREATICOHEPATIC DISEASE*

| AUTHOR | SEX | AGE | LIVER | PANCREAS | GALL BLADDER DISEASE | RED COUNT MILLION | BLOOD PROTEIN GM. % | BLOOD CHOLESTEROL MG. % | DIARRHEA | STOOL | ASCITES ED. EXT | RESULT |
|--------------------------|-----|-----|-------|----------------------|----------------------------|------------------------------|---------------------------|-------------------------------|----------|----------------|--------------------|--------------------|
| Snell and Comfort | M | 36 | Fatty | Stones | - | | 7.2 | 192 | + | Fatty, foul | + | Well, lipocaeic |
| Snell and Comfort | M | 40 | Fatty | Stones | + | 4.2 | Albumin Globulin | 89 | + | Fatty, foul | + | Improved |
| Snell and Comfort | M | 62 | Fatty | Multiple cysts | ? | 3.7 | Albumin Globulin | 75 | + | Fatty, foul | + | Died, au- topsy |
| Norris and associates | F | 68 | Fatty | Fibrosis, atrophy | + | 5.0 down to 3.6 4.1 | Albumin Globulin | | + | Fatty, foul | + | Died, au- topsy |
| Rosenberg | F | 59 | Fatty | ? | + | | | 176 | - | - | - | Well, lipocaeic |
| Cole and Howe | F | 30 | Fatty | Fibrosis, atrophy | + | 3.6 | Albumin Globulin | 135 | - | - | - | Died, au- topsy |

*To be complete this summary should also include cases of pancreatic steatorrhea of infancy and childhood, such as those recently summarized by Anderson.¹¹

Examination of the abdomen revealed a large mass in the right upper quadrant, extending down about 6 cm. below the costal margin. There was moderate tenderness over this mass which presented a smooth surface. Mild hirsutism was present. Her height was 5 feet, 6 inches; weight was 185 pounds. Gastrointestinal series

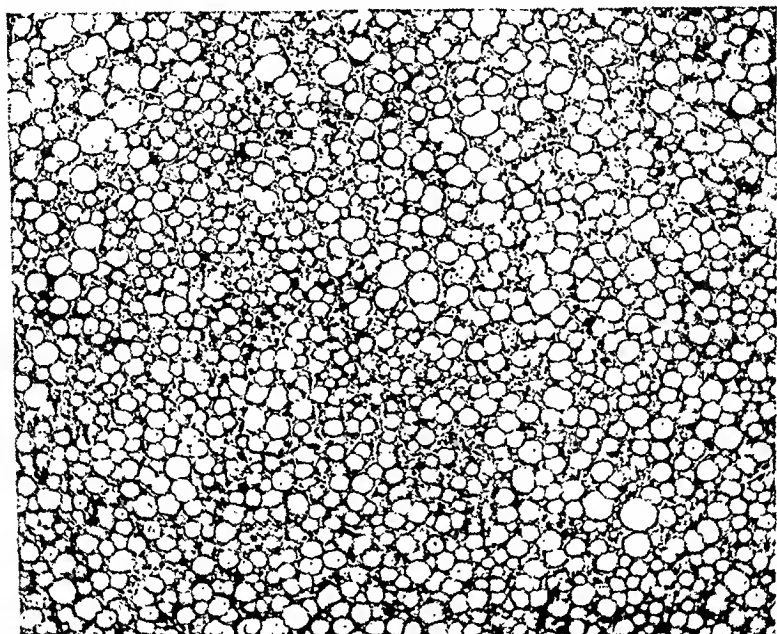


Fig. 1.—Low-power photomicrograph of liver, showing marked fatty infiltration and degeneration. Not enough hepatic cells remain to identify the tissue as liver.

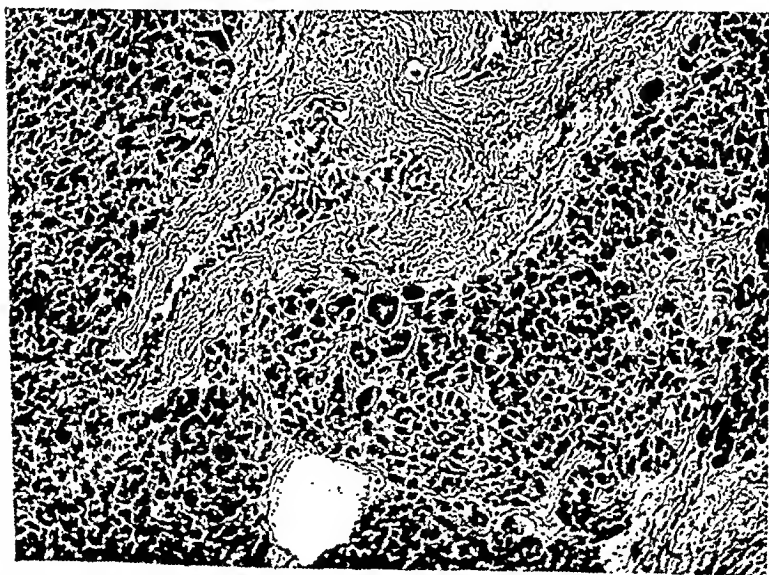


Fig. 2.—Photomicrograph of pancreas, low power, showing distortion of acinar structure with interacinar and intercellular fibrosis. Many cells show degenerative changes and there are several large fat vacuoles present. The picture is one of atrophy and fibrosis.

Higher vitamin requirements in children would explain the higher incidence of pulmonary infection in children, if Andersen's¹¹ suggestion that the pulmonary infection in pancreatic steatorrhea is secondary to a vitamin deficiency is correct.

Therefore, it is our opinion that the pancreatic fibrosis and fatty liver (pancreaticohepatic syndrome) in adults is the same disease as pancreatic steatorrhea (congenital steatorrhea) in infancy and childhood. Differences in the clinical picture of the two conditions are readily explained by the influence of growth requirements in childhood. The pathologic features are even more similar, particularly if we realize that it takes several months for significant fatty infiltration of the liver to take place; we would therefore not expect much fat in the liver of an infant succumbing to the disease at an age under 6 months.

TREATMENT

In view of the splendid contributions of Dragstedt and associates,^{5, 7, 10} one of the most important features in treatment would certainly lie in lipoeic therapy. The prevention of death following pancreatectomy in dogs by feeding vitamins A, B, and D, as noted by Chaikoff,²¹ is in itself sufficient evidence to justify vitamin therapy. Utilization of high carbohydrate and protein diets as indicated may be helpful. The caloric intake should be 20 to 25 per cent above the average requirement, because of the loss of such a large amount of fat in the stool. The use of salyrgan and other drugs should be utilized in symptomatic therapy as indicated. The above remarks on therapy apply also to pancreatic steatorrhea of childhood, particularly the lipoeic therapy. As a matter of fact, on theoretical grounds lipoeic therapy would appear also to be indicated in the idiopathic types of steatorrhea (e.g., celiac disease) since there is presumably pancreatic dysfunction in that group.

REPORT OF CASE

Patient M. R. (No. 56711) was a female 30 years of age, who entered the hospital Sept. 10, 1937, complaining particularly of vomiting of eight weeks' duration. She stated that beginning in about 1922 she developed discomfort in the epigastrium associated with occasional vomiting. Vomiting and discomfort occurred particularly one or two hours after meals. In 1925 the patient had an appendectomy without improvement. Vomiting offered relief. Symptoms became worse until 1930 when she came to Illinois Research Hospital. Gastric analysis at this time revealed total acidity of 50, being elevated to 60 with an Ewald meal. On May 14, 1930, the patient had a laparotomy, at which time a duodenal ulcer was found. The ulcer was annular, stenosing the duodenum and invading the pancreas. A Billroth II type of resection was performed. For two years following operation the patient was completely well. In 1932 she had a severe gastric hemorrhage, but she has had none since. For the past two years she has had intermittent gnawing pain in the epigastrium with occasional attacks of vomiting; this pain radiates to the left and posteriorly, suggesting that it might be of pancreatic origin. Pain is relieved somewhat by alkalis. Ordinarily vomiting relieved the pain, but recently it has not relieved the discomfort which had been even more distressing during the past two months.

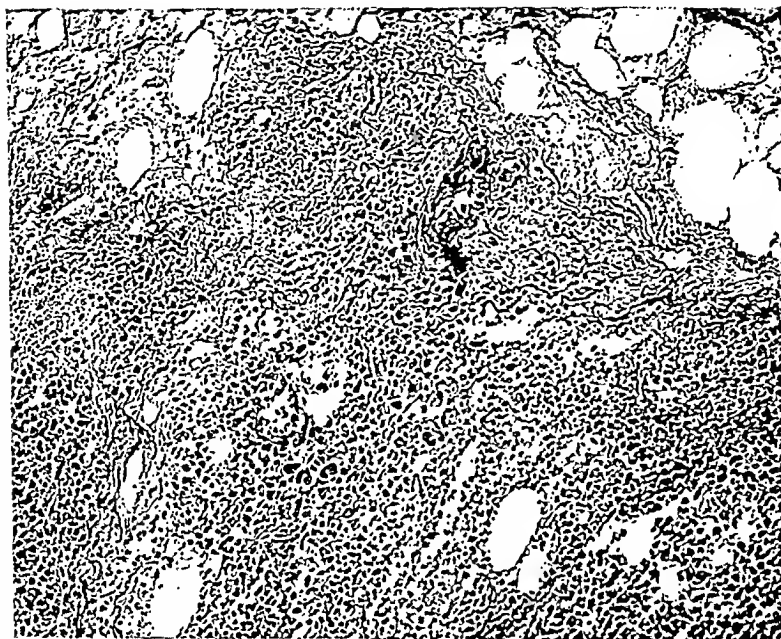


Fig. 3.—Low-power photomicrograph of pancreas, showing necrosis and degeneration of the acinar tissue. The necrosis is so extensive that all cellular detail is lost. In many instances the nucleus is the only structure remaining as identifiable.

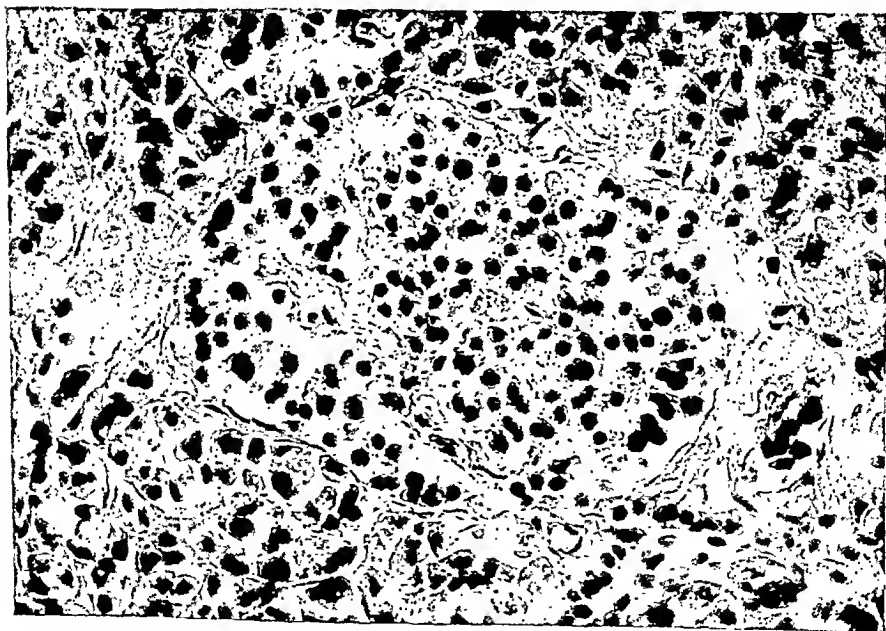


Fig. 4.—High-power photomicrograph of pancreas, showing a relatively normal island of Langerhans. There did not appear to be any significant decrease in the islands, presumably because the islands were more resistant to the necrotizing process.

revealed a gastroenterostomy stoma functioning well. There was no six-hour retention. Cholecystogram revealed no shadow, indicating a pathologic gall bladder. Blood pressure was 125/85. The red blood cell count was 3,600,000. The Kahn test was negative. The fasting blood sugar was 81, N.P.N. 27 and blood chlorides 427. On admission, the patient's serum amylase was 13 (normal 100 to 150). After operation it rose to 255, suggesting that in some way there had been a reactivation of the inflammatory process in the pancreas. The serum albumin was 2 and the serum globulin 2.1, revealing a low albumin level with a tendency to reversal of the albumin-globulin ratio. The icterus index and serum bilirubin were two or three times normal, being 11 and 0.7 respectively. The blood cholesterol was 135 mg. per cent.

Because of the presence of the mass and symptoms, operation was advised and performed on Sept. 20, 1937. The gall bladder was buried in adhesions and contained numerous stones. The liver was enlarged down to the umbilicus, but it had a smooth surface. It was yellowish white in color and, except for position, could not have been identified as liver. Examination of the stomach revealed the closed pyloric end and a gastroenterostomy conforming to the history of a Billroth II operation performed previously. There were numerous adhesions in the region of the stoma which included the colon and some loops of upper ileum. It appeared that a gastro-ecolic fistula was perhaps present, but in view of lack of accurate conformation it was decided not to do anything about it at this time. Realizing that the patient was probably suffering from fatty liver resulting from pancreatic damage, we directed our attention to relieving the pancreas, if possible. Because of the relationship of gall bladder disease to pancreatitis, we decided to remove the badly diseased gall bladder, containing stones. This was done, and the wound closed after a biopsy of the liver was taken. The patient made a rather uneventful convalescence following operation and was allowed up on the sixteenth day. Shortly after being up, she complained of dyspnea and precordial pain. She was put to bed, but dyspnea, cyanosis, and tachycardia persisted in spite of therapy and the signs of acute myocardial failure persisted until her death a few days later, Oct. 10, 1937.

Autopsy Protocol.—The autopsy was performed approximately ten hours after death.

The body was that of a well-developed, moderately obese white woman, 30 years of age, measuring 65 inches in length and weighing 175 pounds. The skin and mucous membranes were a normal color. There was no cyanosis or icterus. There was a slight pitting edema of the lower extremities.

The abdomen was distended. There was a recently healed right pararectus incision 23 cm. in length. The peritoneal cavity contained only a few cubic centimeters of fluid. The intestines were distended and in several places showed perforations, obviously post mortem due to autolysis. The omentum was adherent to the parietal peritoneum at the site of the surgical incision and also to the gall bladder bed. There was no fluid in either pleural cavity and only a few cubic centimeters of clear straw-colored fluid in the pericardial sac. There were no adhesions in the left pleural cavity. In the right pleural cavity there were old fibrous adhesions particularly dense over the lower lobe.

The heart weighed 295 Gm. The subepicardial fat was markedly increased in amount. The myocardium was light yellowish brown, rather soft and flabby, and on the endocardial surface had a mottled yellow "faded leaf" appearance. The right ventricular wall averaged 3 mm. in thickness, but in some areas was thinned to 1 mm. of muscle, while the remainder of the wall consisted of fat. The valve leaflets were normal. The coronary arteries and root of the aorta showed a few scattered fatty plaques measuring up to 2 mm. in diameter.

The lungs were crepitant throughout. Their cut surfaces were moist and reddish purple in color. The larger bronchi contained a small amount of frothy mucus.

pancreatitis is not clear, but presumably it was gall bladder disease including cholelithiasis. Although a jejunoecolic fistula existed, it is difficult to see how this lesion could possibly have been a significant factor in the pathogenesis of the pancreatitis, particularly since considerable space intervened between the fistulous mass and the pancreas. There is much more experimental evidence to point toward a lymphatic communication between the gall bladder and pancreas than there would be between the pancreas and an inflammatory mass such as that produced by the jejunoecolic fistula found in this patient. It is perhaps difficult to explain why there should be such extensive fatty degeneration of the myocardium in a patient only 30 years of age. There was clinical evidence of hepatic insufficiency as borne out by the low serum amylase on admission, a decreased serum albumin with reversal of the albumin-globulin ratio, and a terminal subclinical icterus. The fasting blood sugar was 80 mg. per cent and the urine was negative for reducing sugars. This corresponds well with the histologic observation that the islets of Langerhans were little involved by the necrosis and fibrosis, as well as with the well-known fact that diabetes is rarely the sequel of pancreatitis, even when severe and causing extensive destruction of the pancreas.

The question of the relation of the type and extent of pancreatic pathology to lipocae deficiency is interesting. Dragstedt,⁷ on the basis of experimental work, suggests that lipocae may be elaborated by the alpha cells of the islets of Langerhans and that the lipocae-deficiency syndrome should be fairly common in diabetics. Rosenberg has reported a clinical case of fatty liver with deficient function occurring in a diabetic and improved by the administration of lipocae. It is of interest, however, that his patient had gall bladder colic and was operated upon for hydrops of the gall bladder. Although it is a well-known fact that diabetes is accompanied by considerable infiltration of fat in the liver, it presumably is not capable of resulting in the degree of fatty infiltration illustrated in his case. Obviously, if there was any relation whatever between the diabetes and the patient's disease, the diabetes should be secondary to pancreatic destruction. In Rosenberg's case, as in ours, a definite possible etiologic factor for the development of the pancreatic and liver disease existed; namely, cholecystitis.

In our case the pathology was confined largely to the acinar tissue of the pancreas and, estimating roughly, showed moderate to extreme changes in three-fourths of the pancreatic tissue. The islets appeared normal histologically, though perhaps decreased somewhat in number. On the whole, this case does not appear to support the suggestion of Dragstedt that lipocae is elaborated by the alpha cells of the islets, although it would be entirely possible to have alpha cells deficient in function but showing no abnormality histologically with ordinary stains. Staining for granules in the alpha cells was not attempted because ten hours had elapsed between the time of death and the autopsy.

The liver weighed 4,410 Gm. and was uniformly enlarged to almost three times the normal size. It was firm, finely nodular, light yellowish brown in color, and on cut section the lobular markings were indistinct. The gall bladder had been surgically removed.

The spleen weighed 275 Gm. On section it was soft in consistency, the cut edges everted, and the pulp scraped with moderate ease. The color was reddish purple and the trabeculae and follicles were distinct.

The pylorus was closed by an old operative procedure and there was a patent stoma of a posterior gastrojejunostomy. The transverse colon was closely adherent to the stomach at the site of the gastrojejunostomy. There was a jejunocolic fistula which easily admitted a finger. The stomach contained intestinal contents of a fecal type. There was no evidence of a gastric or jejunal ulcer on careful examination. The remainder of the intestinal tract was normal except for autolytic changes.

The pancreas weighed 49 Gm. and was definitely decreased in size. It was soft, light yellow, and lobulated. Scattered throughout the pancreas were firm white patches measuring up to 3 mm. in diameter.

The kidneys together weighed 375 Gm. The capsules stripped with ease, leaving smooth surfaces. On cut section they were soft and pasty pinkish gray, and the cortical striations were indistinct. In the left kidney there was a bilocular subcapsular cyst filled with clear fluid.

The uterus and adrenals were entirely normal.

Both ovaries showed a few simple cysts, measuring up to 3 mm. in diameter.

Microscopic sections of liver showed the structure almost completely obscured by large vacuoles in the parenchymal cells, so that from the microscopic structure it was difficult to recognize the section as liver. The fat vacuoles were uniformly distributed throughout the section, and sections from different parts of the liver had an identical appearance. In some areas there was a moderate accumulation of small round cells in the portal space.

Microscopic sections of the pancreas from three different areas showed a varying picture. In the white patches described grossly the tissue was entirely necrotic. The nuclear outlines of the acinar cells had completely disappeared and only a dim shadow of the cell structure remained. In other areas the acinar structure was distorted and the individual cells separated by fibrous tissue. Many cells showed atrophic and degenerative changes. There was an increased number of fat cells in the connective tissue stroma. The islets of Langerhans, for the most part, were well preserved and showed less pathologic change than did the acinar tissue. Sections of spleen and adrenal showed no important pathologic changes.

The pathologic diagnosis was: (1) Marked fatty metamorphosis of the liver; (2) fatty infiltration of the myocardium; (3) focal necrosis, atrophy, and fibrosis of the pancreas; (4) old gastrojejunostomy; (5) jejunocolic fistula at the site of the gastrojejunal stoma; (6) healed cholecystectomy; (7) old fibrous adhesions between omentum, parietal peritoneum, and gall bladder bed; (8) parenchymal degeneration of the kidneys; (9) subcapsular cyst of left kidney; (10) old fibrous pleuritis, right.

COMMENT

In our case the fatty infiltration of the liver and the pancreatic fibrosis had progressed to an advanced degree (weight of liver 4,400 Gm.). The immediate cause of death was myocardial decompensation as supported by replacement of heart muscle by fat to such a degree that in places the myocardium was no thicker than 1 mm. In spite of the severe degree of pancreatic destruction, the patient did not have the typical fatty foul stool exemplifying the disease. The etiologic factor causing the

pancreatitis is not clear, but presumably it was gall bladder disease including cholelithiasis. Although a jejunocolic fistula existed, it is difficult to see how this lesion could possibly have been a significant factor in the pathogenesis of the pancreatitis, particularly since considerable space intervened between the fistulous mass and the pancreas. There is much more experimental evidence to point toward a lymphatic communication between the gall bladder and pancreas than there would be between the pancreas and an inflammatory mass such as that produced by the jejunocolic fistula found in this patient. It is perhaps difficult to explain why there should be such extensive fatty degeneration of the myocardium in a patient only 30 years of age. There was clinical evidence of hepatic insufficiency as borne out by the low serum amylase on admission, a decreased serum albumin with reversal of the albumin-globulin ratio, and a terminal subclinical icterus. The fasting blood sugar was 80 mg. per cent and the urine was negative for reducing sugars. This corresponds well with the histologic observation that the islets of Langerhans were little involved by the necrosis and fibrosis, as well as with the well-known fact that diabetes is rarely the sequel of pancreatitis, even when severe and causing extensive destruction of the pancreas.

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In our case the pathology was confined largely to the acinar tissue of the pancreas and, estimating roughly, showed moderate to extreme changes in three-fourths of the pancreatic tissue. The islets appeared normal histologically, though perhaps decreased somewhat in number. On the whole, this case does not appear to support the suggestion of Dragstedt that lipocaic is elaborated by the alpha cells of the islets, although it would be entirely possible to have alpha cells deficient in function but showing no abnormality histologically with ordinary stains. Staining for granules in the alpha cells was not attempted because ten hours had elapsed between the time of death and the autopsy.

It is well known that fatty changes in the liver, more or less marked in degree, may arise from a variety of causes. These include toxins, both endogenous (bacterial) and exogenous (alcohol, chloroform, phosphorus), as well as anoxia (in pneumonias, etc.) which may interfere with the utilization of fats and cause their accumulation to excess in the liver. However, in the patients herein discussed, there appears to be no doubt that the fatty liver was secondary to the pancreatic lesion, particularly after consideration of the experimental data of Dragstedt and others as already discussed.

SUMMARY

During the past two or three years there have been six cases (including our own) reported having a severe grade of fatty infiltration of the liver and fibrosis of the pancreas. There is good evidence, experimental and clinical, that the lesion in the liver is secondary to pancreatic insufficiency. There can be little doubt that the pancreatic steatorrhea of infancy and childhood is the same disease as that exemplified by the six cases herein discussed. Manifestions such as diarrhea with foul bulky fatty stools, weakness, anorexia, nausea, vomiting, epigastric distress or pain and loss of weight are symptoms in common. About the only symptom not seen in each group is osteoporosis, a condition seen occasionally in children suffering from the disease; failure to encounter this in adults is easily explained on the basis of growth demands of childhood. The etiologic factors are unquestionably variable, consisting of congenital malformation of ducts, fetal pancreatitis, and vitamin deficiency in children, and pancreatic stones or gall bladder disease in adults. Whether or not an additional factor, such as a deficiency of some other glandular organ, is necessary for development of the disease cannot as yet be foretold. There is likewise a wide variation in the manifestations of the disease, but certainly no greater than is noted in many other diseases. With the amount of clinical data obtained from a study of the six cases, it now appears that an accurate diagnosis can readily be made without operation or autopsy. Unquestionably, lipocae is very helpful in the treatment of the disease, and may even be curative so long as its administration is maintained at proper intervals.

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THE LATE PHASE OF CONGESTIVE SPLENOMEGALY (BANTI'S SYNDROME) WITH HEMATEMESIS BUT WITHOUT CIRRHOSIS OF THE LIVER

FURTHER OBSERVATIONS ON THE ETIOLOGY OF BANTI'S SYNDROME AND THE EFFECT ON PROGNOSIS OF CERTAIN VARIATIONS IN THE PORTAL VENOUS PATTERN

LOUIS M. ROUSSELOT, A.B., M.D., MED.SC.D., NEW YORK, N. Y.

(From the Departments of Surgery, Presbyterian Hospital and Babies Hospital,
and the Spleen Clinic of the Vanderbilt Clinic)

THE early descriptions of Banti^{1, 2} and his concept of the etiology and clinical course of so-called Banti's disease are so entrenched in medical literature and text that it becomes difficult to alter that which so long has received the sanction of common usage. The following quotation from Cecil³ epitomizes the generally accepted textbook version of the disease: "Splenic anemia (Banti's disease) is a chronic disease of unknown origin, probably toxic, and primary in the spleen, and is characterized by splenomegaly, anemia, and leukopenia, a tendency to gastric hemorrhage, increased formation and destruction of blood cells, and later by cirrhotic changes in the liver, with ascites and jaundice."

The clinical sequence as described by Banti of (1) primary splenomegaly, toxic in origin, (2) an intermediate stage, and (3) finally, the third stage with cirrhosis of the liver, of course, has often been disputed. The German concept of *Stauungsmilz*⁴ was an early attempt to controvert Banti's theory. This in general precludes the possibility of a toxic substance producing primary splenic enlargement and predicates the existence of chronic portal stasis as a precursor of the splenomegaly. It is surprising to find how little convincing evidence has been presented to prove either of the two aforementioned contentions.

The Spleen Clinic of the Presbyterian Hospital has presented a series of papers⁵⁻⁷ in recent years supporting the view that the picture presented by Banti is confusing and misleading in respect to etiology, clinical course, and treatment. Our group is firmly convinced that the etiology of Banti's syndrome may be entirely explained on a mechanical basis; i.e., portal bed obstruction with an associated "portal hypertension."⁸ The site of the obstructive factor causing the portal hypertension and splenomegaly may be intra- or extrahepatic. The term "congestive splenomegaly" suggested by Larrabec,⁹ we believe, is more descriptive than Banti's disease or Banti's syndrome.

The usual intrahepatic lesion producing congestive splenomegaly is, of course, cirrhosis of the liver. This paper, however, is solely con-

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cerned with a selected group of 15 patients, all presenting the typical symptoms, signs, and blood studies usually associated with this syndrome. Severe gastrointestinal bleeding occurred in each of these patients, yet in no case was there coexistent liver cirrhosis. We shall demonstrate that in most of these patients an extrahepatic obstructive factor was present in the portal venous bed. In every instance in which splenic vein pressures were taken at operation, a "portal hypertension" could be determined. The nonexistence of liver cirrhosis in all was established by most of the available methods at our command. These procedures include various liver function tests carried out before operation, gross examination of the liver at operation, and liver biopsy on one or more occasions in the same patient. Furthermore, evidence will be advanced to show that cirrhosis not only was absent at the time of operation, but did not develop as established by the subsequent clinical course and further laboratory studies for varying periods up to nineteen years after operation. In four instances this lack of liver disease has had additional confirmation by autopsy as well.

EVIDENCE DEMONSTRATING THE ABSENCE OF LIVER CIRRHOSIS IN THIS GROUP OF CASES

Table I will clarify the statements as to the nonexistence of liver cirrhosis in all these cases. In the first 2 patients operated upon in 1920 and 1922, there is the least evidence. In each instance there is only the surgeon's operative description of a normal liver. However, in each of the succeeding 13 patients, almost all of whom were operated upon by Allen O. Whipple or myself, at least two forms of corroborative evidence are presented. Histologic proof of normal liver tissue was available in 10 of the 15 cases. Liver biopsy was done at operation in 7 instances and 1 of these also had subsequent autopsy confirmation. Autopsy was also obtained in 3 additional patients who had no liver biopsy at the time of operation.

It is our experience that the bromsulphthalein test is a reliable index of hepatic damage. We have felt particularly secure in our interpretation of these tests because in every case no retention or only a slight trace of the dye was present in the blood after thirty minutes and no equivocal or border line determinations occurred. Bauman and Orr's¹⁰ recent report on the accuracy of the bromsulphthalein test is of interest. In not one instance in our series was there any inconsistency between liver function test, liver biopsy, or necropsy findings.

NATURE OF THE EXTRAHEPATIC LESIONS

As designated in Table I an extrahepatic obstructive factor was demonstrable in the portal venous system of 8 of the 15 patients examined (Cases 4, 5, 6, 7, 9, 11, 12, and 14). This was recognized at the operating table in 4 instances and 4 times it was only demonstrable at autopsy. The failure to discover an obstructive factor in the other 7 cases is not

TABLE I

EVIDENCE OF NONEXISTENCE OF LIVER CIRRHOSIS

| CASE NO. | LIVER FUNCTION STUDIES BEFORE OPERATION | OPERATIONS* | OPERATIVE GROSS APPEARANCE OF LIVER OBSTRUCTIVE FACTORS | FINDINGS | | | AUTOPSY FINDINGS LIVER OBSTRUCTIVE FACTOR |
|----------|--|-------------|---|---------------------------------------|-----------------------------------|---|--|
| | | | | MICROSCOPIC DIAGNOSIS OF LIVER BIOPSY | VENOUS PRESSURE | LIVER FUNCTION STUDIES AFTER OPERATION | |
| 1 | ----- | S | Normal Undetermined | No biopsy | ----- | ----- | ----- |
| 2 | ----- | E | Normal Undetermined | No biopsy | ----- | ----- | ----- |
| 3 | ----- | S | Normal Undetermined | No biopsy | ----- | 13 yr. postoperatively bromsulphthalein test normal Ser. prot. 7.2% Ser. alb. 4.3 Ser. glob. 2.9 | ----- |
| 4 | ----- | S | Normal Undetermined | No biopsy | ----- | 12 yr. postoperatively bromsulphthalein test normal Ser. prot. 6.4% Ser. alb. 4.0 Ser. glob. 2.4 | Normal liver Stenosis of portal vein just below liver |
| 5 | ----- | S | Normal Thrombosis of splenic vein | No biopsy | ----- | ----- | ----- |
| 6 | ----- | S | Normal Undetermined | No biopsy | ----- | ----- | Normal liver Cavernomatous transformation of portal vein |
| 7 | Bromsulphthalein test normal Ser. prot. 5.5% Ser. alb. 3.6 Ser. glob. 1.9 | S | Normal Undetermined | Biopsy: normal liver | ----- | ----- | Normal liver Cavernomatous transformation of splenic and portal veins |
| 8 | Bromsulphthalein test normal Ser. prot. 5.9% Ser. alb. 4.2 Ser. glob. 1.7 | S | Normal Undetermined | Biopsy: normal liver | Splenic V.—370 mm. Artn V.—50 mm. | ----- | ----- |

| | | | | | | | |
|----|---|--------|---|-------------------------|---|--|---|
| 9 | ----- | S | Normal Thrombosis of splenic vein | Biopsy: normal liver | ----- | 2 yr. postoperatively bromsulphthalein test normal Ser. prot. 8.3% Ser. alb. 4.9 Ser. glob. 3.4 | ----- |
| 10 | ----- | S L | Normal Undetermined | Biopsy: normal liver | ----- | 3 yr. postoperatively bromsulphthalein test normal Ser. prot. 6.2% Ser. alb. 4.2 Ser. glob. 2.0 | ----- |
| 11 | Bromsulphthalein test normal Ser. prot. 7.1% Ser. alb. 4.2 Ser. glob. 2.9 | S | Normal Thrombosis of junction of splenic and portal veins | Biopsy: normal liver | Splenic V. 400 mm. Arm V. 170 mm. | ----- | ----- |
| 12 | ----- | S | Not noted Undetermined | No biopsy | ----- | ----- | 1 right lobe, no cirrhosis, focal necrosis present; left lobe represented by small nubbin of tissue Stenosis of lower end of portal, above splenic vein |
| 13 | Bromsulphthalein test normal Ser. prot. 7.7% Ser. alb. 4.4 Ser. glob. 3.3 | S | Normal Undetermined | Biopsy: normal liver | Splenic V. 330 mm. Arm V. 55 mm. | ----- | ----- |
| 14 | ----- | L | Not noted Thrombosis of splenic vein | No biopsy | ----- | 6 yr. postoperatively galactose tolerance test normal Ser. prot. 3.03% Ser. alb. 5.09 Ser. glob. 2.94 | ----- |
| 15 | Ser. prot. 6.9% Ser. alb. 4.3 Ser. glob. 2.6 | S | Normal Undetermined | Biopsy: normal liver | Splenic V. 465 mm. Arm V. 110 mm. | ----- | ----- |

*S, Splenectomy; L, ligation of splenic vessels; E, exploratory celiotomy.

TABLE I
EVIDENCE OF NONEXISTENCE OF LIVER CIRRHOSIS

| CASE NO. | LIVER FUNCTION STUDIES BEFORE OPERATION | OPERATIONS* | GROSS APPEARANCE OF LIVER OBSTRUCTIVE FACTORS | FINDINGS | | | | AUTOPSY FINDINGS LIVER OBSTRUCTIVE FACTOR |
|----------|--|-------------|---|---------------------------------------|----------------------------------|---|--|---|
| | | | | MICROSCOPIC DIAGNOSIS OF LIVER BIOPSY | VENOUS PRESSURE | LIVER FUNCTION STUDIES AFTER OPERATION | | |
| 1 | ----- | S | Normal Undetermined | No biopsy | ----- | ----- | ----- | ----- |
| 2 | ----- | E | Normal Undetermined | No biopsy | ----- | ----- | ----- | ----- |
| 3 | ----- | S | Normal Undetermined | No biopsy | ----- | 13 yr. postoperatively bromsulphthalein test normal Ser. prot. 7.2% Ser. alb. 4.3 Ser. glob. 2.9 | ----- | ----- |
| 4 | ----- | S | Normal Undetermined | No biopsy | ----- | 12 yr. postoperatively bromsulphthalein test normal Ser. prot. 6.4% Ser. alb. 4.0 Ser. glob. 2.4 | Normal liver Stenosis of portal vein just below liver | ----- |
| 5 | ----- | S | Normal Thrombosis of splenic vein | No biopsy | ----- | ----- | ----- | ----- |
| 6 | ----- | S | Normal Undetermined | No biopsy | ----- | ----- | Normal liver Cavernomatous transformation of portal vein | ----- |
| 7 | Bromsulphthalein test normal Ser. prot. 5.5% Ser. alb. 3.6 Ser. glob. 1.9 | S | Normal Undetermined | Biopsy: normal liver | ----- | ----- | Normal liver Cavernomatous transformation of splenic and portal veins | ----- |
| 8 | Bromsulphthalein test normal Ser. prot. 5.9% Ser. alb. 4.2 Ser. glob. 1.7 | S | Normal Undetermined | Biopsy: normal liver | Splenic V.—370 mm. Arm V.—50 mm. | ----- | ----- | ----- |

of the problem has been given a good deal of thought and it is our belief that we may have the answer. It is our purpose to demonstrate that (1) the site of the obstruction and (2) variations in the anatomical distribution of the veins forming the portal system may be the determining factors governing symptomatology, course, and eventual prognosis in any individual case. Referring again to Fig. 1, it seems obvious that a lesion occluding the portal vein close to the liver will impede the flow of a much greater volume of blood than a similar stenotic process located in the splenic vein close to the hilum of the spleen.

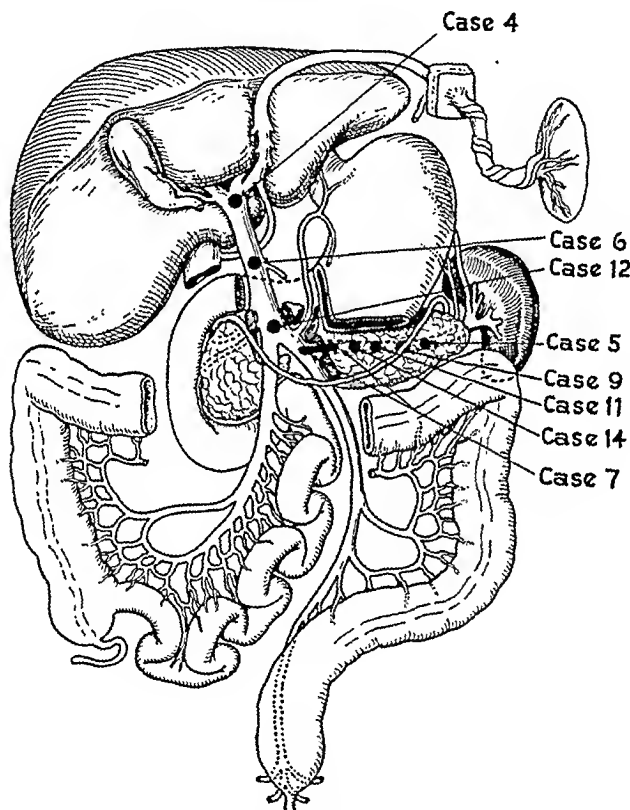


Fig. 1.—Schematic drawing (after F. Paitre, H. Lacaze, S. Dupret), indicating the sites of the obstructive factor in the cases designated.

The former involves the entire return flow of the portal system; whereas, the latter affects only the splenic fraction, or approximately 20 per cent. This question of the site of the obstruction is further qualified, we believe, by the second consideration just alluded to. This second consideration is the variations that occur in the anatomy of the veins forming the portal system.

Fig. 3 portrays six different anatomical patterns taken from six standard sources. Even cursory inspection of these figures will show that an obstructive lesion as indicated in *B* will produce much more profound alterations in intestinal physiology than the identical lesion

necessarily a weakness in our hypothesis but is due rather to the technical difficulties involved in an operative examination of the portal venous bed away from splenic hilum, particularly behind the head of the pancreas.

In this connection it is of interest to note that one patient (Case 4), although reported in two previous papers in 1936 and again in 1939 as having an "obstructive factor" undetermined, has recently died, and a post-mortem examination was made. This patient had had a splenectomy at 5 years of age and was subsequently followed for thirteen years. During this period he continued to have recurring hematemeses and melena and was admitted to the Presbyterian Hospital twenty-four times. Bleeding was always severe and occurred approximately twenty-one times via the esophageal route and ten times per rectum. Because of (1) the normal appearing liver at operation, (2) the normal blood count between bleeding episodes, (3) normal liver function tests at the ninth, eleventh, and twelfth years after splenectomy, we felt secure in our belief that cirrhosis never did exist and that it subsequently had not developed. This patient finally died only seven months ago. Before section was started, one of our staff, William P. Thompson, predicted the finding of a normal liver and also an obstructive lesion in the portal vein close to liver. Both predictions were confirmed.

The nature of the extrahepatic lesions responsible for obstruction to splenic blood in this series are listed as follows:

| | |
|--|---------|
| 1. Thrombosis of splenic vein (traumatic) | Case 5 |
| 2. Thrombosis of splenic at junction with portal vein (traumatic) | Case 11 |
| 3. Thrombosis of splenic vein (nontraumatic) | Case 9 |
| 4. Thrombosis of splenic vein (nontraumatic) | Case 14 |
| 5. Stenosis of portal vein (upper end) just below liver | Case 4 |
| 6. Stenosis of portal vein (lower end) above entrance of splenic vein | Case 12 |
| 7. Cavernomatous transformation of portal vein | Case 6 |
| 8. Cavernomatous transformation of junction of portal vein and splenic veins | Case 7 |

The extrahepatic obstructive lesions just detailed occurred in the respective sites indicated on Fig. 1.

THE ANATOMICAL PORTAL VENOUS PATTERN AS A DETERMINANT OF SYMPTOMATOLOGY AND PROGNOSIS

In an analysis of the long-term results following splenectomy in this entire group, one rather interesting observation has become apparent. From an examination of Fig. 2 it will be seen that 9 of these patients continued to have intestinal bleeding following operation for periods varying from eight months to thirteen years; whereas, 6 were immediately relieved of this serious complication and have remained so for long periods of time, in Case 1 for as long as nineteen years. Why should such a marked variation in clinical behavior occur? This phase

occurring in an individual possessed of a portal system as illustrated in A. Additional observations along these lines will explain many of the vagaries and alterations in clinical behavior in these patients. To quote specific examples from our series:

Case 4 showed a stenotic lesion of portal vein immediately subjacent to liver, and Case 12 lower down in the portal vein. Regardless of the venous pattern in such a situation the entire portal flow is impeded. Splenectomy, although returning the blood picture to normal, will only remove a small burden of the already overloaded collateral circuit. Intestinal bleeding in this type of case, of course, will continue and will not only evolve from esophageal varices but also from small and large bowel. The latter is due to blockage of the superior and inferior mesenteric venous outflow. These are the cases in which melena will always be a dominant feature.

In Cases 5 and 11, however, the obstructive factor was a thrombosis of the splenic vein. This involved only the splenic contribution to the portal flow. Establishment of a collateral circulation via the vasa brevia resulted in bleeding esophageal varices. Following splenectomy, this recurring thrust on the varices was removed. These patients had subsequently no further bleeding. Between these two extremes all gradations in clinical behavior are possible and are dependent, as mentioned before, on (1) the site of the obstruction and (2) the disposition of the accessory veins supplying the portal vein.

SUMMARY

A group of fifteen cases is presented, all with the characteristic features of Banti's syndrome and all with gastrointestinal bleeding as a dominant symptom. Although exhibiting the presumably late symptom of hematemesis, none of these cases had cirrhosis of the liver at operation or subsequently for long periods of time up to nineteen years after operation. The etiology of the splenomegaly can be entirely explained on a mechanical basis with a primary obstructive factor in the portal bed and an associated portal hypertension. The evidence presented therefore contradicts the sequence described by Banti of a primary splenomegaly and a subsequent cirrhosis due to a hypothetical toxic agent.

A variety of extrahepatic lesions have been listed, all capable of producing venous stasis. In the four instances in which splenic vein pressures were determined a definite venous hypertension was recorded. This confirms similar observations previously reported by this clinic in other forms of Banti's syndrome.

The frequency of anomalies in the portal system is stressed.

In this group of cases of congestive splenomegaly due to extrahepatic obstructive lesions, the prognosis and variations in clinical behavior

THE PROPHYLACTIC USE OF SULFANILAMIDE IN ABDOMINAL SURGERY

JOHN S. LOCKWOOD, M.D., AND I. S. RAVDIN, M.D.,
PHILADELPHIA, PA.

(From the Surgical Clinic of the Hospital of the University of Pennsylvania and the Laboratory of Surgical Bacteriology of the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania)

IN VIEW of the dramatically successful results of chemotherapy in such diverse infections as hemolytic streptococcic peritonitis, cellulitis, and septicemia, colon bacillus pyuria, gonococcic urethritis, and pneumococcic pneumonia, the question has logically arisen as to the possible effectiveness of sulfanilamide or one of its derivatives in peritonitis of intestinal origin. The literature on the surgery of the colon has been concerned to a large extent with measures designed to minimize the threat of peritonitis as a complication of such operations. That peritonitis continues to occupy the major position among the causes of death following surgical procedures on the large intestine is shown in Table I. The operative mortality of radical procedures averages about 18 per cent and about 40 per cent of the deaths are due to peritonitis. The data of Rankin⁷ show that, while the mortality following simple colostomy may be very low, almost 60 per cent of the deaths that do occur are attributable to peritonitis. If sulfanilamide can be safely employed to reduce the incidence of postoperative peritonitis, a major advance will have been achieved.

In a previous publication,⁹ dealing with the use of sulfanilamide in hemolytic streptococcic infections, expression was given to the opinion that the effectiveness of sulfanilamide in any lesion is conditioned more by the pathologic character of the infectious process than by the degree of susceptibility of the infecting organisms. As a result of a three-year experience in the use of sulfanilamide in the prevention and treatment of peritonitis on our surgical service at the Hospital of the University of Pennsylvania, we are inclined to reaffirm this opinion. In this paper we will undertake to supply a rational basis for sulfanilamide therapy in polymicrobial peritonitis and to present a summary of our experience to date.

BACTERIOLOGIC CONSIDERATIONS IN PERITONITIS OF INTESTINAL ORIGIN

Peritonitis of intestinal origin is usually a mixed bacterial infection in which the organisms most frequently found are the *Bacillus coli*, the green or nonhemolytic streptococci, and the Welch bacillus. The careful studies of Meleney, Harvey, and Zaytseff-Jern¹⁰ on the bacterial flora of peritonitis, in which sound bacteriologic methods were used, showed

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are dependent on two factors: (1) the site of the obstructive lesion and (2) variants in the anatomy of the venous pattern. To the best of our knowledge, this latter concept is herein presented for the first time.

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Presented at the meeting of the Society of University Surgeons at New York, N. Y., February 9 and 10, 1940.

B. coli in 87 per cent, hemolytic and nonhemolytic streptococci in 7 per cent and 21 per cent respectively, green streptococci in 49 per cent, and *Clostridium welchii* in 38 per cent. The disease was more severe and the mortality higher when more than one type of organism was present. That the interplay of synergisms among these bacteria was an important factor in the pathogenesis of peritonitis was further emphasized by the experimental studies of Meleney, Olpp, Harvey, and Zaytseff-Jern.¹¹ In their experiments mice succumbed when small fractions of the lethal doses of individual strains of *B. coli*, streptococci, and *Cl. welchii* were mixed prior to intraperitoneal inoculation. These organisms as they exist in feces are probably saprophytic rather than parasitic, deriving their essential nutrition from the fecal contents rather than from the host tissues. Before they can shift from the saprophytic phase to the parasitic or invasive phase, the ground usually has been prepared by primary injury or loss of blood supply in some area of the bowel. The proteolysis of tissue which takes place in such an injured area provides the bacteria with an environment in the tissues themselves which is suited to their needs, and invasion of the bowel wall and later of the peritoneum itself may occur. In postoperative peritonitis necrosis of tissue at the suture line or leakage of fecal contents into the peritoneal cavity is the most frequent initiating factor. After the adaptation of intestinal bacteria to the parasitic state has been achieved, they may then continue to multiply in tissues wherein primary necrosis has not occurred. The form of peritonitis most frequently encountered, of course, is that resulting from appendicitis. In this type of peritonitis the bacteria have successfully bridged the existing gap between the saprophytic state of intestinal bacteria and the parasitic state of bacteria involved in an invasive lesion, the necrosis of the appendix itself being the most important factor involved in this change. A peritoneal defense quite adequate to deal with avirulent saprophytes may be quite overwhelmed if these same organisms have become toxin-producing parasites by multiplying in necrotic tissue. We wish merely to re-emphasize the well-known fact that whether or not peritonitis results from fecal contamination incident to a colon anastomosis probably depends as much on the amount of necrosis at the suture line as on any other consideration. It may be assumed that spreading peritonitis will not develop unless the contaminating bacteria encounter in the bowel wall or peritoneum an environment capable of supplying to them the nutritive materials required for their multiplication and toxin production.

METHODS OF REDUCING INCIDENCE AND MORTALITY OF PERITONITIS

The risk of postoperative peritonitis in surgery has probably been substantially lowered by the institution of a number of improvements in surgical technique and management. Among these improvements the most important are: (1) atraumatic methods of anastomosis and the use of silk for seroseros sutures; (2) preliminary enterostomy with

preoperative decompression and cleansing of the bowel; (3) intubation with the Miller-Abbott double lumen tube to minimize tension proximal to the suture line; and (4) mobilization of the peritoneal defense prior to a radical operation.

It has been suggested that a factor in the lower mortality of multiple-stage procedures might be the "vaccination" of the peritoneum incident to the first stage. The recent studies of Collier and his associates¹² on dogs showed that the peritoneum was somewhat more resistant to infection by large doses of *B. coli* two weeks after a prececostomy had been performed than the peritoneum of normal dogs or of dogs four weeks after such an operation. The magnitude of the protection was not as great as that provided by the intraperitoneal injection of colibactragen (Steinberg)* forty-eight hours before infection.

There is little unanimity of opinion as to the value of intraperitoneal injection of substances such as coli-bactragen designed to mobilize the cellular defense of the peritoneum preoperatively. The experimental studies of Gay¹³ and of Steinberg¹⁴ have emphasized the importance of the large macrophages and the polymorphonuclear cells in the protection of serous membranes against invasive infection. These cells accumulate rapidly following the injection of sterile irritants. Since phagocytosis is presumably the chief defense mechanism of the peritoneum, there is theoretical support for the desirability of increasing the numbers of available phagocytes. Furthermore, it may be that a more rapid sealing of serosal surfaces of an anastomosis would take place if the peritoneum were mildly irritated and hyperemic. Dixon,¹⁵ of the Mayo Clinic, is one of the strong advocates of peritoneal protection. He has reported a mortality of 6 per cent in 180 resections in vaccinated patients, as against 17 per cent in a "similar series" of unvaccinated cases. Rankin, who formerly advocated vaccination on the strength of an improved mortality record during a period in which it was used, now attributes the good results to the more careful preoperative decompression which was instituted at the same time. He has recently reported¹⁶ 130 cases in which no vaccine was used with an 8.4 per cent mortality. Collier and Rife¹⁷ and Oehsner and DeBakey⁸ believe that the vaccine should be introduced at the time of operation only in those cases where soiling has occurred during resection and anastomosis. They believe this to be preferable to preoperative vaccination. In our experience the pain incident to the preoperative vaccination has appeared to constitute a real disadvantage. We have not employed this procedure in the cases included in this report.

SULFANILAMIDE IN PERITONITIS

It is now generally agreed that sulfanilamide owes its effectiveness in infections to its capacity to limit the multiplication of bacteria, although

*Coli-bactragen is a mixture of killed colon bacilli, aleuronat, and tragacanth.

there is considerable disagreement as to the precise mechanism by which bacteriostasis is induced. Many factors operate to influence the magnitude of the sulfanilamide effect, among them the most important being: (1) the size of the inoculum; (2) the concentration of the drug; (3) the presence or absence of leucocytes; (4) the chemical state of the medium, with particular respect to its content of split products of protein; and (5) the susceptibility of the organisms, varying almost as much among strains as among species. While the influence of these modifying factors is most clearly brought out in in vitro experiments, there is reason to believe that similar modifying influences usually obtain in vivo.

In the type of peritonitis which follows operations on the large bowel most of these factors are adjusted in such a way as to allow a drug effect of considerable magnitude. The size of the bacterial inoculum is relatively small, many of the organisms even in feces being dead or devitalized; a satisfactory concentration of drug in the peritoneal fluid may be rapidly obtained with parenteral or oral administration of the drug;¹⁸ leucocytes are present in abundance, particularly if peritoneal protection has been instituted; and, unless a considerable amount of devitalized tissue has been left at the site of the anastomosis, there would be a minimal amount of protein-split products in the peritoneal fluid. Few data are available with respect to the susceptibility to sulfanilamide of the bacteria usually encountered in this form of peritonitis. The colon bacillus is highly susceptible to the concentrations of the drug which occur in the urine, and, in vitro, the drug has a definite effect on this organism in urine when the concentration is only 10 mg. per cent, provided protein-split products are excluded.¹⁹ On the other hand, the nonhemolytic streptococci as a group are comparatively resistant to sulfanilamide bacteriostasis. The *Streptococcus fecalis* (Lancefield Group D) infections of the urinary tract do not respond as favorably to sulfanilamide as do most other types. Perhaps the major question involved in the successful application of sulfanilamide therapy to the mixed infections of the peritoneum is whether relative insusceptibility of the bacteria to the drug may be compensated for by a coincidence, on the favorable side, of all of the other factors tending to modify the drug effect. For example, the staphylococcus is ordinarily quite resistant to sulfanilamide in soft-tissue infections, but in the urinary tract, or in human serum with a small inoculum of staphylococci, high degrees of bacteriostasis may be demonstrated provided the concentration of drug is high and protein-split products are excluded.¹⁹

We are now engaged in an experimental study of the protective value of sulfanilamide in experimental infections of mice with mixtures of the ordinary intestinal bacteria. The experimental details will be presented in a later publication.

TABLE I

INCIDENCE OF PERITONITIS AS A CAUSE OF DEATH IN MORTALITY FOLLOWING OPERATIONS FOR LARGE BOWEL CARCINOMA

| AUTHOR | NO. OF CASES | LOCATION | TYPE OF OPERATION | MORTALITY | | DUE TO PERITONITIS |
|-----------------------------------|------------------|------------------|--|-----------|------|--------------------|
| | | | | CASES | % | |
| Wilkie ¹ | 101 | Colon | Anastomosis or Mikulicz | 15 | 14.8 | 13.3 |
| Patterson and Webb ² | 63* | Colon | Mikulicz | 12 | 19.0 | 16.7 |
| Stone and Mc-Lanahan ³ | 166 | Colon and rectum | Anastomosis or abdominal perineal | 23 | 13.8 | 47.8 |
| Mayo and Simpson ⁴ | 204 | Transverse | Mikulicz, anastomosis, or palliative | 33 | 16.1 | 63.6 |
| Allen ⁵ | 653 | Colon and rectum | Anastomosis, Mikulicz, or abdominal perineal | 110 | 16.8 | 30.0 |
| MacFee ⁶ | 156 | Colon | Anastomosis or Mikulicz | 34 | 21.8 | 55.8 |
| Rankin ⁷ | 969 | Colon and rectum | Colostomy | 42 | 4.3 | 57.1 |
| Ochsner and DeBakey ⁸ | Collected series | Colon | Anastomosis or Mikulicz | 412 | | 41.7 |

*Excluding 7 unfavorable cases.

Accounts of the experience gained from the use of sulfanilamide therapy in the treatment of local and diffuse peritonitis of appendiceal origin have been published by Corry, Brewer, and Nicol²² and by Ravdin, Rhoads, and Lockwood.¹⁸ The mortality of acute appendicitis in these two series before and since the institution of sulfanilamide (for the severe cases) is shown in Table II. It is recognized that

TABLE II

THE MORTALITY FROM ACUTE APPENDICITIS AND ITS COMPLICATIONS

| | TOTAL CASES | DEATHS | DRAINED (%) | GROSS MORTALITY (%) |
|--|-------------|--------|-------------|---------------------|
| <i>Service E—Hospital of the University of Pennsylvania:</i> | | | | |
| Before the use of sulfanilamide (to 1936) | 552 | 8* | 37.0 | 1.4 |
| With the use of sulfanilamide in cases showing infection outside the appendix (1936 to 1940) | 318 | 1† | 41.0 | 0.3 |
| Total | 870 | 9 | 38.0 | 1.0 |
| <i>Corry, Brewer, and Nicol: Brit. M. J. 2: 561, 1939:</i> | | | | |
| Before the use of sulfanilamide (1934-1938) | 1,131 | 60 | | 5.3 |
| With the use of sulfanilamide in cases of peritonitis (1938-1939) | 273 | 3‡ | | 1.1 |
| Total | 1,404 | 63 | | 4.5 |

*One death occurred in a patient not operated upon.

†This patient did not receive sulfanilamide until two days after operation.

‡Twenty-six patients with "general peritonitis" (including all 3 deaths) and 15 with "abscess" and removal of appendix were treated with sulfanilamide and its derivatives.

one is justified in reserving judgment as to the statistical significance of these figures. However, it may be pointed out that the only death in our treated group was a patient who did not have peritonitis at the time of operation and who died as a result of separation of the stump ligature and massive soiling of the peritoneum. Sulfanilamide was not started until the third day after operation, when widespread infection was present. It was on the basis of our conviction that sulfanilamide had been a factor in saving the lives of a few desperately sick patients in this group that we were encouraged to make a trial of the drug in the prevention and treatment of other types of peritonitis. It appeared that sulfanilamide should be even more effective in preventing postoperative peritonitis than in treating the established disease. In appendiceal peritonitis all of the above-mentioned factors influencing the magnitude of the sulfanilamide effect except that of drug concentration may be unfavorably adjusted; even though the necrotic appendix may be removed, it is impossible always to evacuate necrotic exudate on the peritoneal surfaces and the leucocytic exudate at the time of operation may be already overwhelmed by the number of actively multiplying bacteria (Steinberg's tertiary stage²³).

During 1938 we started using sulfanilamide in the treatment of inflammatory and traumatic bowel perforations. We and our associates were so impressed with the recovery of some of these cases that we started using prophylactic sulfanilamide in all of our bowel resections. The volume of material does not warrant our presenting it as a statistical study. Instead, we have elected to include in the three accompanying tables all of the cases of these types in which sulfanilamide has been used. Tables III and IV present a consecutive series of 22 colon resections of various types, 16 in cases of carcinoma and 6 in nonmalignant lesions. The type of operation performed in each case varied with the location and extent of the lesion and the condition of the patient. Ileocolostomy, employing open technique, was used in 6 instances. In all of the other cases the involved bowel was removed and one or both ends of the resected intestine were brought out through the abdominal wall as a terminal or a double-barrel colostomy. In one case (No. 40929) the tumor had invaded the jejunum, necessitating resection of a segment of jejunum. The continuity of the small intestine was restored by side-to-side anastomosis. In Case 41646 the tumor had perforated and a small abscess was opened during the process of removing the mass. In Case 43211 resection was carried out for a lesion of the cecum which proved pathologically to be an acute diverticulitis. Spiking temperature, chills, and jaundice appeared on the fifth day, two days after stopping sulfanilamide. Although the blood culture was negative, the existence of suppurative pyelophlebitis seemed probable. Rapid improvement occurred after drug administration was resumed. Ottenberg and Berek²⁵ have al-

ready reported the recovery under sulfanilamide treatment of two cases of suppurative pylephlebitis.

There were no deaths from peritonitis in the group of twenty-two resections and in no case was there clinical evidence of peritonitis during the postoperative course. The one death which occurred (Case 43236) was due to coronary occlusion on the first postoperative day. This series is small and of doubtful statistical significance. However, in view of the usual incidence of peritonitis as a cause of death in bowel resection, as shown in Table I, we have naturally been encouraged by the results of prophylactic sulfanilamide therapy during this first year of its trial. Our impression of the probable value of the drug in these cases is fortified through our previously cited experience in the treatment of peritonitis following appendicitis.

The toxic drug reactions which occurred in three cases were mild in character and responded to stopping the treatment.

Infection of the abdominal wound occurred in four cases. It is possible that these wound infections might have been prevented if treatment had been continued for longer periods of time. The cellular defenses of the peritoneum rapidly may complete the destruction of contaminating bacteria which are inhibited by sulfanilamide. Bacteria in an abdominal wound, however, are protected against the maximal drug effect by the presence of products of tissue proteolysis and may grow out and cause infection if chemotherapy is continued for only a brief period.^{9, 10}

Table V presents 6 instances of inflammatory and traumatic perforation of the intestinal tract in which sulfanilamide treatment was used. The recovery of the two patients with local peritonitis associated with sigmoid diverticulitis is perhaps not at all remarkable, but they are included in the interest of keeping the series complete. In the other 4 cases the nature of the lesions found at operation and the immediate condition of the individual patients was such as to lead us to believe that the prognosis was extremely grave. Case 42924, a 70-year-old man with widespread peritonitis from a ruptured diverticulitis of the right colon, lived long enough to develop a localized pelvic abscess, which was drained, but he died three weeks following the initial operation, from myocardial failure.

Surgeons have been hesitant to employ sulfanilamide and its derivatives in the prevention and treatment of peritonitis of intestinal origin. This has been due to a well-entrenched belief that sulfanilamide is effective only in infections due to certain cocci, particularly the hemolytic streptococcus. It is our impression that under special experimental or pathologic conditions which favor drug action, sulfanilamide may have some degree of antibacterial effect against almost all species of pathogenic bacteria and that the pathologic character of the lesion is of greater importance in conditioning the magnitude of the drug effect

TABLE
PROPHYLACTIC SULFANILAMIDE

| HOS- PITAL NO. | AGE | ADMIS- SION DATE | DATE OF DIS- CHARGE | DIAGNOSIS | OPERATION | |
|----------------------|-----|------------------------|---------------------------|---|--------------------|--|
| | | | | | DATE | TYPE |
| 43252 | 65 | 10/24/39 | 11/26/39 | Carcinoma of cecum with metastasis to liver | 11/11/39 | Ileocolostomy |
| 42654 | 63 | 7/10/39 | 8/10/39 | Carcinoma of cecum | 7/11/39 | Ileocolostomy; resection of cecum and right colon, one stage |
| 43464 | 70 | 11/22/39 | 1/24/40 | Carcinoma of cecum | 11/25/39 | Lahey-Bloch-Mikulicz resection |
| 41125 | 49 | 1/24/39 | 2/15/39 | Carcinoma of ascending colon | 1/31/39 | One-stage ileocolostomy and resection |
| 43236 | 65 | 10/31/39 | 11/ 5/39 | Carcinoma of ascending colon | 11/ 4/39 | Lahey-Bloch-Mikulicz resection |
| 40232 | 56 | 10/ 1/38 | 10/22/38 | Carcinoma of ascending colon | 10/ 6/39 | Ileocolostomy (first stage of resection) |
| 42139 | 52 | 5/29/39 | 7/ 5/39 | Carcinoma of hepatic flexure | 6/ 1/39 | Mikulicz resection |
| 40929 | 51 | 1/30/39 | 3/22/39 | Carcinoma of transverse colon with involvement of jejunum | 1/31/39 2/23/39 | Cecostomy Resection of colon and jejunum (Devine) |
| 22671 | 67 | 6/14/39 | 7/ 5/39 | Carcinoma of descending colon | 6/17/39 | Obstruction resection (Rankin) |
| 37419 | 68 | 3/13/39 | 4/ 8/39 | Carcinoma of sigmoid | 3/23/39 | Resection and colostomy, first stage |
| 44202 | 51 | 12/18/39 | 1/21/40 | Carcinoma of sigmoid | 12/21/39 | Obstruction resection (Rankin) |
| 43004 | 47 | 9/11/39 | 10/ 2/39 | Carcinoma of sigmoid involving uterus | 9/12/39 | Mikulicz resection; partial hysterectomy |
| 41646 | 53 | 4/ 8/39 | 5/ 1/39 | Carcinoma of sigmoid | 4/ 8/39 | Resection and colostomy, first stage; lesion perforated |
| 41977 | 71 | 5/10/39 | 6/20/39 | Carcinoma of rectum | 5/13/39 | Lockhart-Mummery; peritoneum opened |
| 40935 | 51 | 1/ 2/39 | 2/14/39 | Carcinoma of rectosigmoid | 1/ 7/39 | First stage abdominal perineal |
| 41515 | 60 | 3/15/39 | 4/18/39 | Carcinoma of rectum | 3/21/39 4/ 1/39 | Colostomy Perineal excision |

*h, Hypodermoclysis; p.o., by mouth.

III

IN COLON RESECTIONS

| SULFANILAMIDE | | DAYS OF DRUG | COMPLICATIONS | COURSE | REMARKS |
|---------------------------------|-----------------------------------|--------------------|---|--|---|
| PRE- OPERA- TIVE (GM.) | POST- OPERA- TIVE (GM.)* | | | | |
| 4.0 | 16.0 h. | 4 | Hematoma of wound | Very smooth; out of bed ninth day | |
| 3.2 | 9.6 h. 4.0 p.o. | 4 | Chill with temperature to 104° fourth day; wound infection | Smooth except for wound infection | |
| 4.0 | 16.0 h. | 5 | | Smooth | |
| 4.0 | 19.2 h. | 4 | None | Normal T.P.R. after fifth day; smooth | |
| 6.5 | 6.4 h. | 1 | Coronary occlusion | | Died |
| | 9.6 h. 24.0 p.o. | 8 | None | Very smooth; highest temperature 100.6° | |
| 4.0 | None | - | None | Smooth; temperature normal after ninth day | |
| | 14.4 h. | 4 | None | Smooth | |
| 1.5 | 29.1 h. | 5 | None | Highest temperature 100.4° on second day | Second stage was a very involved dissec- tion requiring three hours |
| | 16.0 p.o. | 3 | None | Very smooth; highest temperature 100.4° on eighth day | |
| 6.0 | 16.8 h. 12.0 p.o. | 6 | Drug fever sixth day | Satisfactory | |
| | 10.8 h. 17.0 p.o. | 6 | None | Smooth | |
| | 24.0 p.o. | 4 | Jaundice on fourth day | Temperature elevated for 6 days | Cause of jaundice un- known; possibly sul- fanilamide; cleared up after stopping drug |
| | 22.4 h. | 4 | Anemia; slight jaundice; ? pulmonary infarct | Stormy 4 days; tempera- ture to 102.4° second day | |
| 4.0 | 9.6 h. 12.0 p.o. | 6 | Urinary retention and cystitis; drug fever fifteenth day (second course) | Temperature to 101.4° first day; normal after third until drug fever | |
| | 17.3 h. | 6 | Acute anemia; ? drug fever | Late temperature rise to 102.4° on fourth and fifth days | Anemia and fever prob- ably due to drug |
| | 34.0 p.o. | 8 | Small hemorrhage in per- ineal wound | Smooth; temperature to 102° on second day | |

TABLE

PROPHYLACTIC SULFANILAMIDE IN THE

| HOSPITAL NO. | AGE | AD-MISSION DATE | DATE OF DIS-CHARGE | DIAGNOSIS | OPERATION | |
|--------------|-----|-----------------|--------------------|--|-----------|-------------------------------------|
| | | | | | DATE | TYPE |
| 43181 | 53 | 10/21/39 | 11/25/39 | Chronic ulcerative colitis; multiple polyposis | 10/28/39 | Ileostomy; resection right colon |
| 43181 | 53 | 12/15/39 | 1/25/40 | Chronic ulcerative colitis; multiple polyposis | 12/19/39 | Resection left colon |
| 43211 | 36 | 10/25/39 | 12/13/39 | Acute diverticulitis of cecum | 10/25/39 | Resection of cecum (Mikulicz) |
| 36886 | 22 | 4/10/39 | 5/ 2/39 | Terminal ileitis | 4/13/39 | Ileocolostomy, one stage; resection |
| 42844 | 45 | 9/ 5/39 | 9/26/39 | Terminal ileitis | 9/ 9/39 | Ileocolostomy, one stage; resection |
| 41722 | 33 | 10/26/39 | 11/28/39 | Lymphopathia venerea; previous colostomy | 11/ 8/39 | Resection of sigmoid and rectum |

*h, Hypodermoclysis; p.o., by mouth.

TABLE

PROPHYLACTIC SULFANILAMIDE

| HOSPITAL NO. | AGE | AD-MISSION DATE | DATE OF DIS-CHARGE | DIAGNOSIS | OPERATION | |
|--------------|-------|-----------------|--------------------|--|-----------|---|
| | | | | | DATE | TYPE |
| 39053 | 61 | 4/28/38 | 6/ 4/38 | Acute sigmoid diverticulum; perforation following enema; generalized peritonitis; belly full of soapbuds | 5/ 5/38 | Colostomy with exteriorization of perforation |
| 43157 | | 9/12/39 | 10/21/39 | Perforation of esophagus by esophagoscope; cardiospasm | 9/12/39 | Repair of perforation; splenectomy |
| 42924 | 70+ | 9/16/39 | 10/ 9/39 | Ruptured diverticulitis of right colon; diffuse peritonitis | 9/16/39 | Drainage |
| 40982 | 52 | 12/27/38 | 1/10/39 | Sigmoid diverticulitis; local peritonitis | 12/27/38 | Exploratory laparotomy and drainage |
| 40220 | 8 mo. | 8/30/38 | 9/ 6/38 | Perforated Meckel's diverticulitis | 8/30/38 | Exploratory laparotomy; diverticulectomy; no drainage |
| 40687 | 51 | 11/30/38 | 12/21/38 | Acute sigmoid diverticulitis; local peritonitis | 11/30/38 | Drainage |

*h, Hypodermoclysis; p.o., by mouth.

IV

NONMALIGNANT LESIONS OF THE COLON

| SULFANILAMIDE | | DAYS OF DRUG | COMPLICATIONS | COURSE | REMARKS |
|----------------------------|------------------------------|--------------------|--|---|--|
| PREOP- ERATIVE (GM.) | POSTOP- ERATIVE (GM.)* | | | | |
| 2.0 | 18.4 h. 3.0 p.o. | 5 | Phlebitis twelfth day | No abdominal complications; up on tenth day | Signs of pylephlebitis disappeared rapidly after resumption of sulfanilamide |
| | 10.8 | 2 | Infected wound | Febrile | |
| | 23.2 h. 28.0 p.o. | 3 7 | ? Pylephlebitis on fifth day; jaundice, chills and fever | | |
| | 25.6 h. 4.0 p.o. | 6 | None | T.P.R. normal third day; very smooth | |
| | 14.4 | 3 | Minor wound infection | T.P.R. normal fourth day; very smooth | |
| 5.0 | 6.4 h. 13.0 p.o. | 5 | Wound infection | Smooth | |

V

IN BOWEL PERFORATIONS

| SULFANILAMIDE | | DAYS OF DRUG | COMPLICATIONS | COURSE | REMARKS |
|----------------------------|------------------------------|--------------------|---|---|--|
| PREOP- ERATIVE (GM.) | POSTOP- ERATIVE (GM.)* | | | | |
| | 28.8 hypo. 5.0 p.o. | 7 | Drug fever fifth day | Temperature below 100° for five days | |
| | 28.8 hypo. | 3 | Wound infection | Febrile | Culture: Hemolytic <i>Staph. aureus</i> and nonhemolytic streptococcus |
| | 24.0 hypo. | 5 | Pelvic abscess (drained 10/5/39); cardiac failure | Gradual failure after three weeks; no peritonitis | Died |
| | 16.6 h. 9.0 p.o. | 6 | None | Very smooth | Culture: staphylococcus |
| | 7.2 h. | 3 | None | T.P.R. normal after third day; very smooth | Culture: staphylococcus |
| | 17.6 hypo. 13.2 p.o. | 7 | None | Very smooth | Culture: Nonhemolytic streptococcus and <i>Str. viridans</i> |

than the considerations of bacteriologic specificity. In peritonitis a minimal drug effect against the intestinal pathogens may serve to augment the natural defenses of the peritoneum to the extent that the balance of factors will become favorable to the host. There is no evidence available to justify the employment of sulfanilamide prophylactically or therapeutically to the exclusion of any other recognized principles or practices of therapy. We believe that the weight of experimental and clinical evidence now justifies the use of sulfanilamide as an adjunct to other forms of treatment in the management of threatened or established peritonitis of intestinal origin.

SUMMARY

1. In spite of important advances in technique peritonitis remains an important cause of death following operative procedures on the large intestine.

2. Peritonitis of intestinal origin is a polymicrobie infection, and the bacteria concerned in its production are relatively, but not entirely, resistant to sulfanilamide bacteriostasis.

3. This bacteriostatic effect may become significant in the peritoneal defense against postoperative peritonitis if an adequate concentration of drug is present, if the number of contaminating organisms is small, if tissue necrosis is minimal, and if the usual cellular defense is present.

4. Clinical experience is as yet insufficient to warrant final conclusions as to the effectiveness of sulfanilamide in the prevention of peritonitis.

5. A series of sulfanilamide-treated cases is presented in which it is suggested that the drug may safely be used in conjunction with other therapeutic measures of recognized value. None of these cases showed evidence of spreading peritonitis after the institution of sulfanilamide therapy.

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THE REPAIR OF TRACHEAL AND BRONCHIAL DEFECTS WITH FREE FASCIA GRAFTS

MAX TAFFEL, M.D., NEW HAVEN, CONN.

(From the Department of Surgery, Yale University School of Medicine)

IN 1909 Kirschner⁴ published his first extensive communication describing the many possible uses of free homologous grafts of fascia. In the immediately subsequent years Hohmeier,^{2, 3} Davis,¹ Kostenko and Rubaschew,⁵ and Neuhof⁶ reported experimental studies where free grafts of fascia had been employed to cover defects in the cervical trachea. A window of varying size was made in the anterior wall of the trachea and this was at once covered with a rectangular flap of fascia sewn securely in place at the margins of the defect. In addition Hohmeier³ performed tracheotomies in two of his animals, and, after a period of twelve and thirteen days respectively, débrided the slightly infected edges of the tracheal opening and sutured a patch of fascia over it. The wounds in both instances healed per primam. Hohmeier^{2, 3} alone derived his grafts from the fascia of the sternocleidomastoid muscle. The other authors turned to the fascia lata. In 1912 Levit⁶ and later Lucas⁷ and Neuhof⁸ each reported a clinical case of a long-standing tracheal fistula which had been successfully repaired with a segment of fascia lata.

The purpose of these experiments was to reopen the subject concerning the employment of fascia grafts in repairing defects of the respiratory tree, to study histologically and at varying time intervals the nature of the repair, and to determine whether such a graft could be utilized in the closure of tracheal and bronchial defects within the thorax. Four series of experiments were carried out, all in dogs: (I) Repair of cervical tracheal defects; (II) repair of bronchial defects; (III) repair of bronchial defect after lobectomy; (IV) repair of tracheal defect after total pneumonectomy.

Series I. Repair of Cervical Tracheal Defects (Six Animals).—Under intravenous nembutal anesthesia the trachea was exposed through a midline incision in the lower neck. A rectangular full thickness segment of the anterior tracheal wall, measuring 1 by 1 cm. and including arcs of one or two tracheal rings, was excised. The open window was covered with a slightly larger free patch of deep cervical fascia which was sutured to the outer surface of the trachea at a distance of about 3 mm. from the margins of the defect. The sutures did not penetrate the lumen of the trachea and were placed in such a way as to make the fascia span tightly across the defect. There was thus no fluttering of the graft with the phases of respiration. Interrupted sutures of fine

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black silk placed closely together were used. An airtight closure, determined by flooding the wound with salt solution, was obtained in each instance, and the wound was sutured in layers without drainage. All the animals survived the procedure and remained perfectly well throughout the duration of the experiments. The wounds healed per primam. In no instance were any respiratory complications or subcutaneous emphysema noted. The animals were sacrificed at the end of one, two, three, four, eight, and twelve weeks respectively. Immediately before death, the wounds in the neck were opened and the operative sites in the trachea exposed. The new tissue filling the defect in each instance was firm and did not flutter.

Dog 429 was sacrificed after one week. *Gross Findings.*—The pre-tracheal museles are loosely adherent to the trachea at the site of the defect. The graft is easily identified and is firmly in place. It has lost the usual appearance of fascia and now presents as a flat sheet of semiopaque brown-red finely granular tissue completely covering the tracheal defect and projecting hardly at all into the lumen of the trachea. The inner aspect of the graft is bare and naked of epithelium except at its very borders where a thin edge of new epithelium is growing in from the tracheal mucosa. The rest of the trachea, the bronchi, and the lungs in this animal as well as in all the others in this series reveal no evidence of any inflammatory reaction.

Microscopic Findings.—The graft appears to have lost its usual cytological architecture and is represented as a poorly delimited sheet of homogeneous pink-staining tissue containing scattered pyknotic vestiges of former nuclei. Invading the periphery of the graft and completely covering its external surface is a rich growth of fibroblasts which contains within it many newly formed, thin-walled blood vessels and a heavy sprinkling of polymorphonuclear leucocytes and round cells. The central core of the graft is as yet free from this invasion. The luminal surface is covered with a layer of fibrin sparsely infiltrated with polymorphonuclear leucocytes. There is some regeneration of the mucosa at the edges of the defect. The new epithelial cells are flatter than usual, and no cilia are seen. Two silk sutures, cut in cross section, are surrounded by a thin wall of fibroblasts and leucocytes.

Dog 428 was sacrificed after two weeks. *Gross Findings.*—The trachea is not unduly adherent to the adjacent museles. The defect is completely covered by red, granular, vascular tissue. The epithelium, which has now regenerated over the entire inner surface of the graft, appears to be definitely thinner than that of the adjacent mucosa. The defect has not shrunken appreciably in size, and there is at no point any diminution in the caliber of the trachea.

Microscopic Findings.—The epithelium has completely regenerated and covers the entire defect except at one point near its center where

it appears to have been brushed away in the process of preparing the section. The cells are flat to cuboidal. Definite cilia are seen in the new mucosa, but these are sparse. No submucous glands are present. The original graft is not recognizable, and the defect is filled with a thick vascular layer of fibroblasts which are beginning to resemble adult connective tissue cells. There is a scattered infiltration everywhere, including the new mucosa, of polymorphonuclear leucocytes and round cells. This is most marked in the outer surface of the trachea, well outside the zone of the defect, where several small and large clusters of leucocytes and fibroblasts encapsulate the cut ends of silk sutures. Here occasional multinucleated giant cells are seen. New budding cartilage cells are growing from the cut ends of the rings adjacent to the defect.

Dog 425 was sacrificed after three weeks. *Gross Findings.*—The tracheal window, unaltered in its dimensions, is closed with a firm layer of pale red tissue which does not project into the lumen of the viscus. The epithelium has completely regenerated. There appear to be no remains of the original fascial stamp.

Microscopic Findings.—No definite traces of the graft can be discerned. The defect is bridged with a layer of loose vascular areolar tissue which now closely resembles adult connective tissue. The cellular infiltration is still present but is very much diminished in extent. On the outer surface of the trachea at some distance from the edge of the defect a few large clusters of polymorphonuclear leucocytes are present. Silk strands are found within some of these. The mucosa has completely regenerated. The cells are flat to cuboidal in shape, but abundant cilia are present. A few subepithelial mucous glands and three small islands of young cartilage cells are in evidence in the new subepithelial connective tissue near the borders of the defect.

Dog 423 was sacrificed after four weeks. *Gross Findings.*—The defect is well covered with a pale white tissue resembling connective tissue. The mucosal surface of the trachea everywhere appears to be normal and intact.

Microscopic Findings (Fig. 7).—No distinct traces of the graft are present. There is complete regeneration of the epithelium which is arranged in the typical pseudostratified formation and is no longer distinguishable from the normal previously intact epithelium. Filling the defect is a layer of well-differentiated adult connective tissue scattered within which are a moderate number of blood vessels and occasional areas of differentiating fibroblasts. The cellular infiltration is still present, but it is not conspicuous. Foreign body reactions are seen surrounding fragments of silk sutures in the outer tracheal wall. There are a few islands of regenerating cartilage cells and mucous glands in the new submucosa.

Dog 422 was sacrificed after eight weeks. *Gross Findings.*—The pretracheal muscles are quite adherent to the trachea. The defect is filled with a thin layer of white avascular translucent tissue. The epithelium is intact.

Microscopic Findings.—Normal adult relatively avascular connective tissue spans the defect. Cellular infiltration is minimal. The new mucosal lining is made up of the usual ciliated tracheal epithelium with an abundance of goblet cells. Some silk strands encapsulated by connective tissue cells are seen. A few scattered fibers of the adherent pretracheal muscles are noted.

Dog 374 was sacrificed after twelve weeks. The gross and microscopic (Fig. 11) findings are essentially identical to those described in Dog 422.

Series II. Repair of Bronchial Defects (Six Animals).—Under intravenous nembutal anesthesia supplemented with intermittent administration of positive pressure through an indwelling intratracheal tube, the left hemithorax was entered through an incision in the fourth left interspace anteriorly. The main left upper lobe bronchus was identified and a full thickness rectangular segment measuring 0.5 by 0.5 cm. excised. The defect was bridged in the same manner as described in Series I with a free flap of deep fascia removed from the chest wall, care being taken to ensure an airtight closure. In some instances a small bit of striated pectoral muscle was applied to reinforce the closure. The left lung was then expanded and the wound in the pleura and chest wall closed without drainage. All the animals survived the procedure. The wounds healed per primam. No respiratory difficulties of any nature were encountered. There were no instances of hydrothorax, pyothorax, or tension pneumothorax. The animals were sacrificed at the end of one, two, three, four, eight, and twelve weeks respectively. Before removing the anterior chest wall, the lungs were inflated in situ with air, and the trachea clamped. The same gross findings were observed in the six animals of the series. All the lobes of the lungs were fully and normally expanded and filled their respective pleural cavities. The left upper lobe was pink and crepitant with no foci of atelectasis or pneumonic infiltration. There was no free fluid in either pleural cavity. The wound in the parietal pleura at the fourth left interspace healed well and did not become adherent to the left lung. The lungs and tracheo-bronchial tree were removed en masse. A solution of 10 per cent formalin was injected into the trachea in an amount sufficient to distend the lungs to approximately their usual size within the thoracic cavity. The trachea was then ligated and the entire pulmonary system submerged in formalin and allowed to fix.

Dog 411 was sacrificed after one week. *Gross Findings.*—There is no encroachment of the left upper lobe bronchial lumen at the site of the defect. The graft can be recognized, but it is dull, opaque and granular

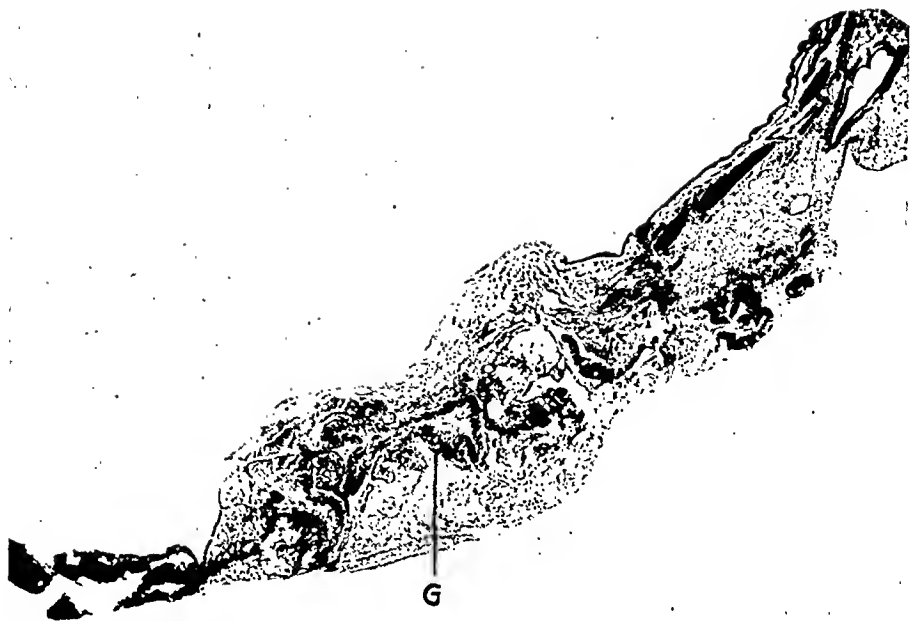


Fig. 1.—Dog 411. Bronchus window (one week). Graft (G) visible as wavy, opaque fragmented structure surrounded by proliferating fibroblasts, inflammatory cells, and adipose tissue. Early regeneration of the mucosa is noted at the edges of the defect. ($\times 6$.)

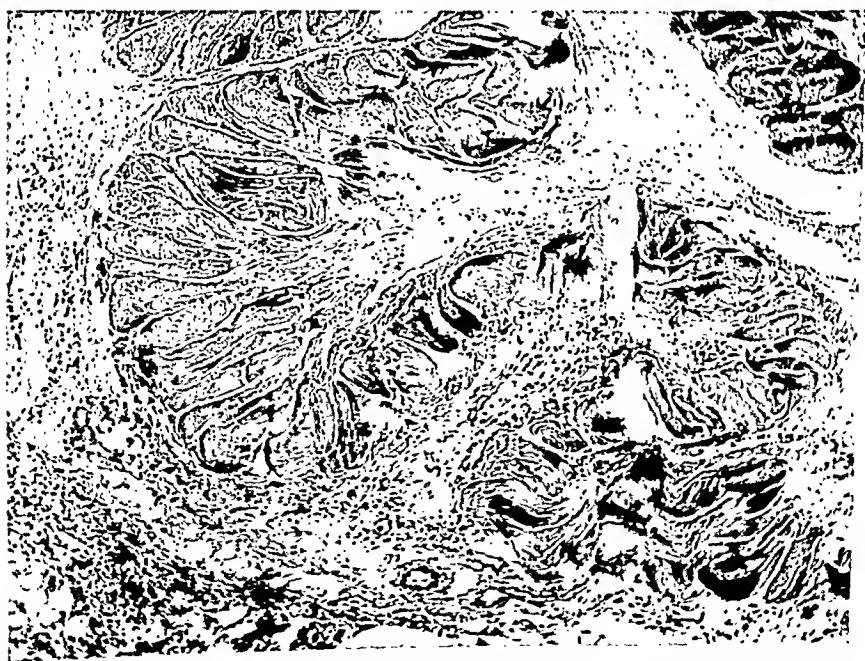


Fig. 2.—Dog 411. Bronchus window (one week). Graft is dull and fragmented and appears hyalinized. Growing into it from all sides are fibroblasts infiltrated with polymorphonuclear leucocytes and round cells. ($\times 75$.)

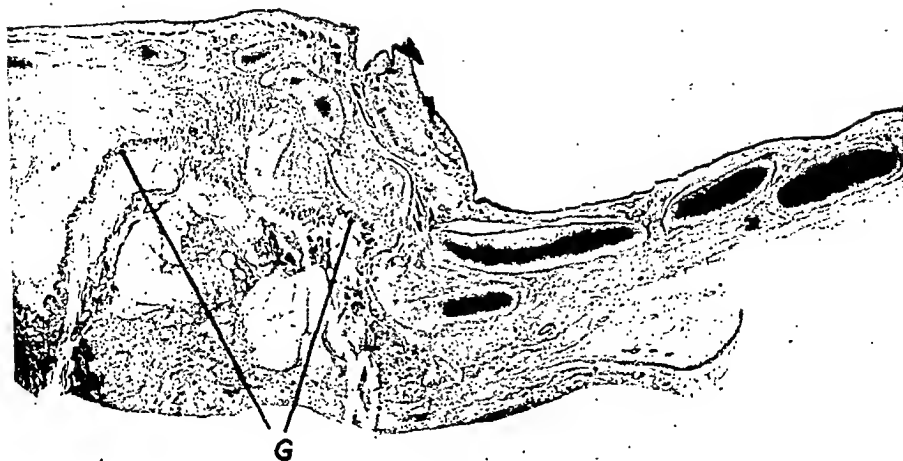


Fig. 3.—Dog 417. Lobectomy (one week). Epithelium completely regenerated. Marked proliferation of new cartilage. Remainder of defect filled with granulation tissue and fat-containing cells. Graft (G) presents as thin, wavy, shredded structure. ($\times 6.5$.)

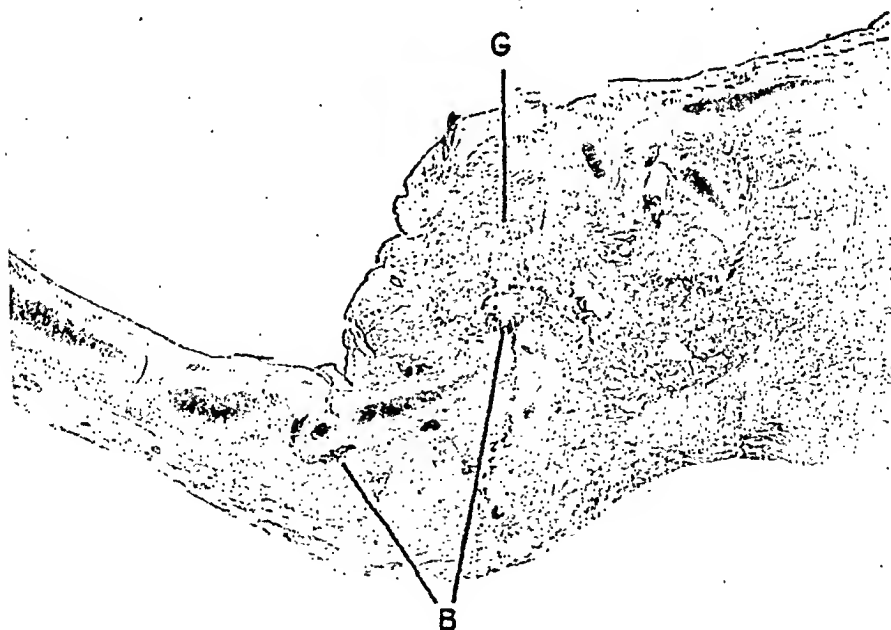


Fig. 4.—Dog 416. Lobectomy (two weeks). Mucosa regenerated. Graft (G) being invaded and replaced by fibroblasts. Defect filled with differentiating fibroblasts and islands of adipose tissue. Silk sutures (B). ($\times 7.5$.)

and does not resemble the former pale stamp of connective tissue. The mucosal surface of the graft is raw and covered with fibrin.

Microscopic Findings (Figs. 1 and 2).—The graft is easily identified and does not appear to be viable. It takes a diffuse homogeneous pink stain and contains scarce nuclear elements. It is surrounded by a layer of invading fibroblasts and young, newly formed blood vessels. A marked infiltration of polymorphonuclear leucocytes and round cells is present in these invading zones as well as among the fibroblasts surrounding strands of silk sutures. There are scattered groups of large fat-containing cells. Early and limited regeneration of epithelium is noted only at the margins of the defect, while the inner aspect of the remainder of the graft is covered with very vascular granulation tissue over which lies a sheet of fibrin heavily infiltrated with white cells.



Fig. 5.—Dog 410. Bronchus window (two weeks). Graft (G) with outlines poorly defined, being replaced by proliferating fibroblasts. ($\times 125$.)

Dog 410 was sacrificed after two weeks. *Gross Findings*.—The bronchial lumen is free and not constricted. The graft cannot be recognized, and the gap is filled with a flat layer of brown-red vascular tissue. The bronchial mucosa is everywhere intact.

Microscopic Findings (Fig. 5).—The mucosa is completely regenerated. It is composed of pseudostratified ciliated columnar epithelium and contains many goblet cells. Beneath this new mucosa is a layer of fibroblasts loosely arranged and harboring within it many thin-walled blood vessels and few leucocytes. There is no evidence of regeneration

of the muscularis mucosa. The fascia graft is fragmented, takes a homogeneous pink stain, and appears hyalinized. Each fragment is surrounded and invaded by fibroblasts heavily infiltrated with polymorphonuclear leucocytes and round cells. A few strands of silk are similarly being invaded. Several clusters of fat-containing cells are present.

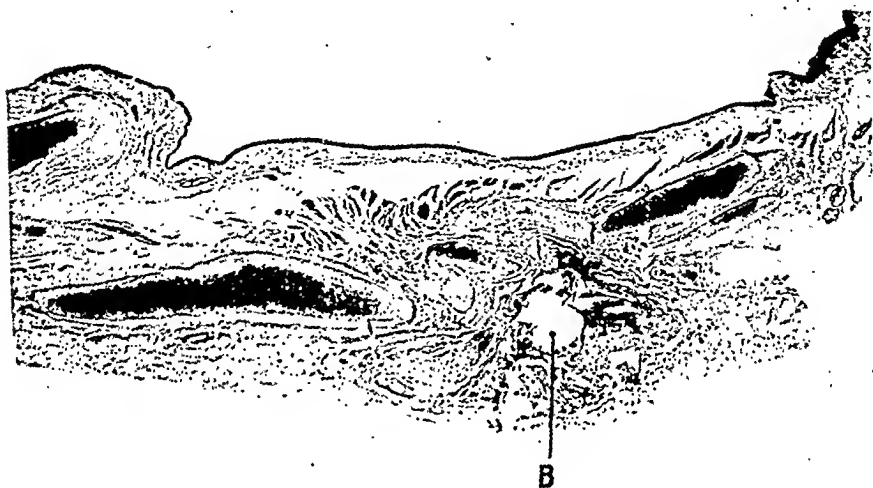


Fig. 6.—Dog 414. Lobectomy (three weeks). Mucosa regenerated. Smooth muscle cells in submucosa are prominent. New islands of cartilage are present. B represents shredded black silk suture. There is no evidence of graft. (X17.)



Fig. 7.—Dog 423. Tracheal window (four weeks). Respiratory epithelium completely regenerated. Defect filled with differentiated adult connective tissue. Cellular infiltration not prominent. (X11.)

Dog 409 was sacrificed after three weeks. *Gross Findings.*—The lumen of the bronchus is not narrowed. The original defect appears to be shrunken somewhat in size and is covered with a sheet of red-brown tissue, the inner surface of which is completely epithelialized.

Microscopic Findings.—The pseudostratified ciliated columnar epithelium is completely regenerated and rests upon a layer of young connective tissue cells. No muscularis mucosa is present here. In the area of the defect there are scattered fragments of thin viable adult connective tissue which are partially encircled by fibroblasts and fat-containing cells. These fragments appear to be the remains of the original graft which have "taken." The cellular infiltration is in general less conspicuous, while scattered foreign body multinucleated giant cells are present in large numbers within islands of granulation tissue near strands of silk. At the borders of the defect there are a few small scattered clumps of young cartilage.

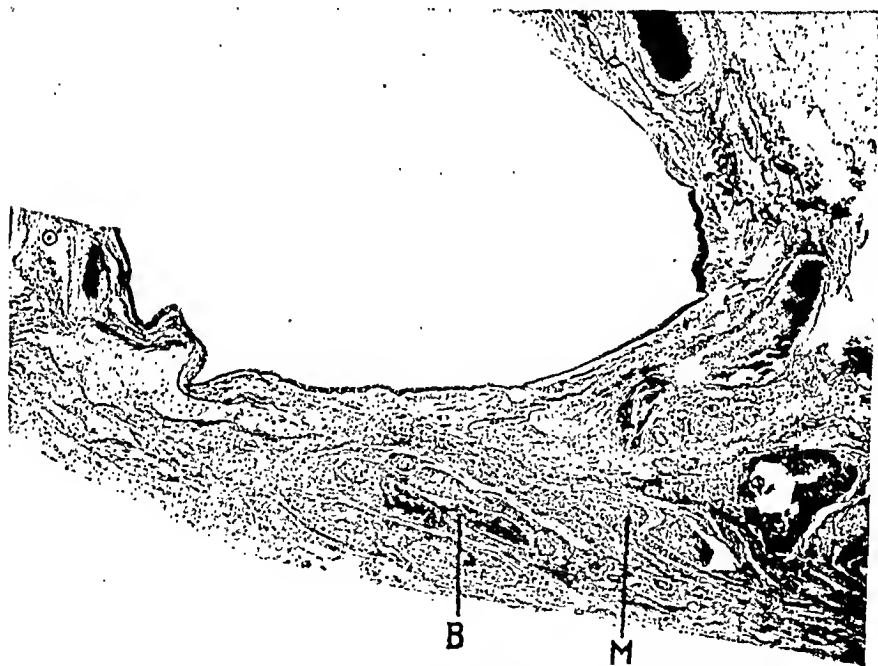


Fig. 8.—Dog 407. Bronchus window (four weeks). Mucosa intact and rests on layer of connective tissue. Fibroblasts and wandering cells noted chiefly around sutures (B). Well-stained fibers of striated muscle (M) are present. (X12.)

Dog 407 was sacrificed after four weeks. *Gross Findings.*—The mucosa is intact. The defect is spanned by a thin layer which resembles connective tissue in its gross characteristics.

Microscopic Findings (Fig. 8).—Under the completely regenerated epithelium there is a layer of normal adult connective tissue and a moderate amount of adipose tissue. Mucous glands and a few islands

of young cartilage cells are present in the new submucosa, but no smooth muscle elements can be clearly recognized. The cellular infiltration is almost completely absent and, together with differentiating fibroblasts, is limited to the areas immediately adjacent to strands of silk. At one point near the border of the defect some viable, well-stained fibers of striated muscle are noted.

Dog 398 was sacrificed after eight weeks. *Gross Findings.*—A thin layer of translucent connective tissue which contains elements of cartilage spans across the defect. The mucosa is intact.

Microscopic Findings (Fig. 9).—A layer of adult connective tissue fills the defect. In addition there is a striking proliferation of young cartilage cells which have overgrown from the edges and almost meet in the center of the defect. The epithelium is ciliated and completely regenerated. The submucosa is composed of connective tissue and contains mucous glands but no smooth muscle. Silk strands encapsulated by a thin collar of connective tissue and small round cells are present.

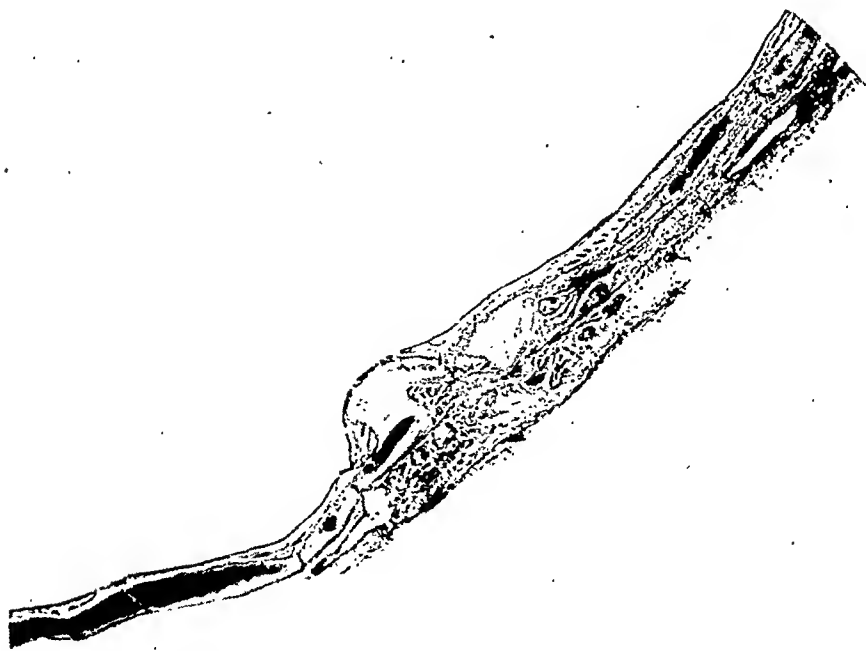


FIG. 9.—Dog 398. Bronchus window (eight weeks). Mucosa regenerated and lifted by marked overgrowth of new cartilage. Adult connective tissue present everywhere except immediately adjacent to black silk sutures where few fibroblasts are still noted. ($\times 9$.)

Dog 387 was sacrificed after twelve weeks. The gross and microscopic (Fig. 12) findings are essentially the same as those described for Dog 398. The marked proliferation of cartilage is not noted here. There is no evidence of any new growth of the muscularis mucosa.

*Series III. Repair of Bronchial Defect After Lobectomy (Six Animals).—*The anesthesia and operative approach were the same as those described in Series II. The left upper lobe pulmonary arteries and veins were isolated, doubly ligated, and divided. A clean transection of the left upper lobe bronchus was made exactly at its bifurcation from the

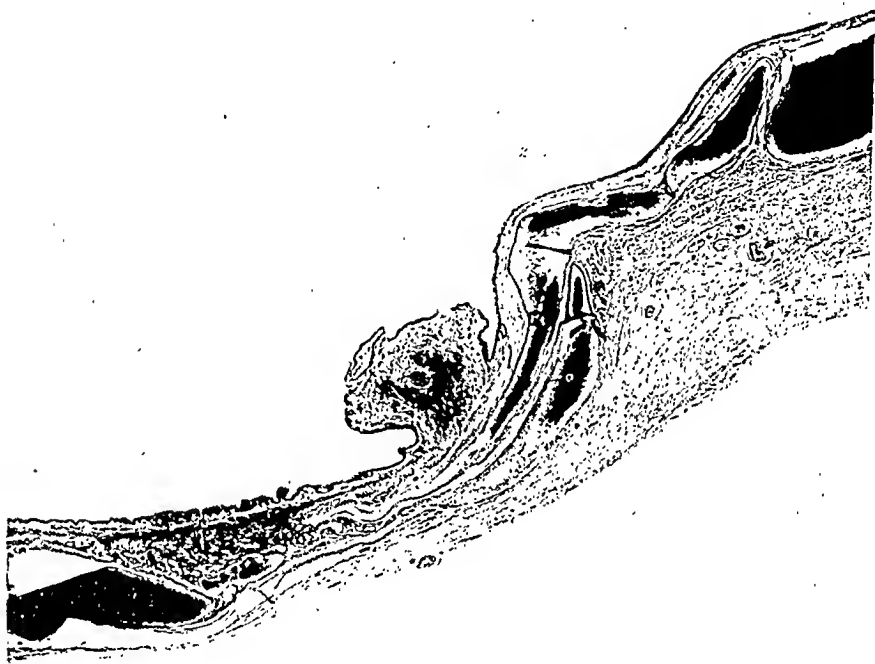


Fig. 10.—Dog 426. Pneumonectomy (eight weeks). Defect spanned by connective tissue into which there has grown at one side a tongue of new cartilage. Mucosa intact. The projecting submucosal tuft of granulation tissue harbors a silk suture in its center. (X11.)



Fig. 11.—Dog 374. Tracheal window (twelve weeks). Mucosa intact and resting upon layer of connective tissue. A few sutures are seen. (X11.)

left main bronchus and the left upper lobe was removed. A patch of deep thoracic fascia was sewn securely over the open hole, care being taken to make the closure airtight. The left lower lobe was allowed to expand, and the wound in the chest wall was repaired in layers without drainage. The dogs survived the procedure without developing any complications. The wounds healed per primam. No respiratory difficulties were encountered at any time. The animals were sacrificed at the end of one, two, three, four, eight, and twelve weeks respectively. As in Series II, the lungs were inflated in situ with air and the trachea clamped, prior to opening the thoracic cage. All the animals exhibited essentially the same gross findings. The empty nest of the left upper



Fig. 12.—Dog 387. Bronchus window (twelve weeks). Normal mucosa and connective tissue across defect. (X17.)

lobe was filled in part by the overexpanded left lower lobe and in part by the similarly overexpanded right upper lobe which, together with its adjacent mediastinum, had crossed the midline and herniated into the left upper thoracic cavity. These changes in the realignment of the lobes of the lung were noted as early as one week after the operation and were indeed almost complete at that time. The left lower lobe was always well expanded and revealed no evidence of inflammatory infiltration. No blood or free fluid was found in either of the pleural cavities. There were no adhesions between the left lower lobe and the parietal pleural wound. After removal from the thorax the lungs were inflated with 10 per cent formalin and fixed in this position.

The gross and microscopic findings in this group were essentially the same as those noted in Series II and therefore will not be described in detail. There appeared in this third series to be a greater shrinkage of the size of the defect than was observed in either of the other two groups. Regeneration of the mucosa was complete by the end of the first week (Fig. 3). The epithelium was ciliated and pseudostratified, and contained numerous goblet cells. In addition there seemed to be a greater growth of new cartilage, which for the first time seemed to take an active part in filling the defect. The muscularis mucosa was quite abundant in the new submucosa, but whether this was due to an actual proliferation of smooth muscle cells or to their possible displacement from the adjacent normal submucosa could not be determined. The progressive changes in the graft were the same as those described previously. The animals in this group were Dogs 417, 416 (Fig. 4), 414 (Fig. 6), 413, 412, and 406 (Fig. 13).



Fig. 13.—Dog 406. Lobectomy (twelve weeks). Regenerated mucosa covering thick layer of connective tissue. The many silk sutures cut in cross section are surrounded by thin collars of differentiating fibroblasts and wandering cells. ($\times 11$.)

Series IV. Repair of Tracheal Defect After Total Pneumonectomy (Two Animals).—The anesthesia and the operative approach were the same as those described in Series II and III. The left main pulmonary arteries and veins were isolated, separately ligated, and divided. The main left bronchus was transected exactly at the point where it branched

off from the trachea, and the left lung was removed. No bronchial stump remained. A stamp of deep thoracic fascia was sewn securely over the open defect in the trachea, and the wound in the chest wall was closed without drainage. Both animals survived the procedure and made uneventful recoveries. The wounds healed per primam. The animals were sacrificed at the end of eight and twelve weeks respectively.

Dog 426 was sacrificed after eight weeks. At autopsy the right lung was inflated with air, and the trachea was ligated in the neck before removal of the chest wall.

Gross Findings.—The left diaphragm is elevated, and the bony thoracic wall on this side is slightly shrunken. The heart lies entirely within the left hemithorax. The remainder of this half of the thoracic cavity is filled largely with the overexpanded right upper lobe which has herniated across the midline, and to a lesser extent with the overexpanded right lower and mediastinal lobes. There is no free fluid within the pleural cavities. The wound in the left parietal pleura is completely healed and is not adherent to any of the underlying thoracic viscera. The lobes of the right lung are all overexpanded and are soft and crepitant throughout. The defect at the bifurcation of the trachea is spanned by a layer of brown-red translucent tissue, the inner aspect of which is completely epithelialized. There is at no point any appreciable encroachment upon the lumen of the trachea or the right main bronchus.

Microscopic Findings (Fig. 10).—The ciliated pseudostratified epithelium is completely regenerated. The submucosa is moderately thick and contains many mucous glands and a heavy infiltration of polymorphonuclear leucocytes and round cells. The inflammatory cells are prominent chiefly in the neighborhood of the sutures. External to the submucosa is a relatively avascular layer of adult connective tissue cells and new cartilage. The original graft cannot be recognized. A small submucosal tuft of granulation tissue with a silk suture at its core is noted.

Dog 424 was sacrificed after twelve weeks. The gross findings are the same as those described for Dog 426. On microscopic examination the defect is found to be covered with a layer of adult connective tissue cells. Cellular infiltration is scant and inconspicuous. The normal respiratory mucosa is completely regenerated. A few scattered mucous glands are present in the submucosa and occasional black silk sutures are noted.

SUMMARY AND CONCLUSIONS

Free fascia grafts have been successfully employed in dogs to repair defects in the trachea and bronchi after local resection of full thickness segments of these viscera as well as after lobectomy and total pneumonectomy. The twenty animals investigated all survived the operative procedure and remained entirely well throughout the duration of the experi-

ment. The wounds healed per primam. There were no instances of subcutaneous emphysema, pneumothorax, hydrothorax, or pleural empyema. None of the animals developed any pulmonary parenchymal complications that could be detected during life or at autopsy. A moderate diminution in the size of the defect was noted only in the lobectomy experiments. In the other series the original measurements of the defect remained essentially unchanged. There was in none of the animals any appreciable encroachment upon the caliber of the trachea or bronchus at the site of the application of the graft.

The healing process followed essentially the same pattern whether the defect was in the trachea or the bronchus. The graft did not appear to remain viable but acted rather as a temporary and airtight scaffold quickly to be invaded and replaced by wandering cells and proliferating fibroblasts. The latter in turn became differentiated into collagen-bearing adult connective tissue which remained as a permanent supporting structure spanning the defect. Regeneration of the respiratory mucosa, already in evidence at the borders of the defect after one week, was complete at the end of the second week. The cells, at first cuboidal in shape and sparsely ciliated, quickly assumed the pseudostratified appearance and acquired their normal complement of cilia and goblet cells. In one instance (Dog 417, lobectomy) complete epithelialization occurred within one week. Mucous glands were noted in the new submucosa after the third week. There was no clear evidence in any of the sections of regeneration of the muscularis mucosa. Budding young cartilage cells were observed in the cut ends of the tracheal and bronchial rings. These islands of new cartilage, however, with a few notable exceptions, appeared to take little part in filling the original defect. The silk sutures were at the outset encapsulated by fibroblasts and wandering cells, and later by a thin shell of adult connective tissue. All phases of healing were practically complete during the fourth week after the application of the graft. The new and final structures which served to restore the continuity of the viscus were composed of (1) an inner layer of pseudostratified ciliated epithelium; (2) a layer of submucosa with occasional mucous glands and a few small islands of new cartilage but, with occasional exceptions, no fibers of muscularis mucosa; and (3) an outer layer of supporting adult connective tissue.

There are obvious inherent advantages in a method which provides an airtight and adequate closure of an open defect in the wall of a hollow semirigid respiratory tube without the necessity of approximating the free edges of the defect to each other and without constricting to any appreciable degree the caliber of the viscus. Certain clinical applications of this method at once suggest themselves. Its usefulness in the repair of old tracheotomy wounds in man has already been pointed out. Small benign and early malignant lesions of the trachea, which for one reason or another cannot be adequately treated through

the bronchoscope, may be resected and the opening covered with a stamp of fascia. Similarly benign lesions of the larger bronchi may be excised locally and the remaining defect closed with fascia, thus obviating the necessity of extirpating the accompanying normal pulmonary lobe. Its greatest field of usefulness appears at the moment to be in those instances of lobectomy or total pneumonectomy where it is necessary to transect the bronchus exactly at its point of bifurcation from the main bronchus or the trachea respectively and where no long bronchial stump is left that can be closed by the usual methods. The closure of such an opening by suturing the edges to each other may not only be difficult technically because of the rigidity of the viscus, but may result in a serious kinking and obstruction at the site of the suture. Finally free fascia grafts may be employed to advantage to cover and reinforce ordinary suture lines in the trachea or larger extrapulmonary bronchi. Fascia is present everywhere in abundance, and an amount sufficient for a free graft is readily available in the local operative wound.

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IS THE CONSERVATIVE TREATMENT OF INFECTION OR GANGRENE IN DIABETIC PATIENTS WORTH WHILE?

HERMAN E. PEARSE, M.D., AND HROLFE R. ZIEGLER, M.D.,
ROCHESTER, N. Y.

(From the Department of Surgery of the University of Rochester School of Medicine and Dentistry)

THE conservative treatment of peripheral arterial disease seeks to avoid leg amputation. This objective has been held by members of our surgical staff who were interested in the subject, and any method which offered hope of improvement was tried. This has been of obvious benefit in some disorders but has not been so apparent in the diabetic group, for these patients have many complicating factors present that may influence the outcome. It was considered desirable to appraise our results in patients with diabetes.* We wished to see when and where our treatment was satisfactory, how it could be improved, where it had failed, and how the failures could be avoided. These data are presented, without comparative analysis or review of the literature, only to show our experience and to act as a guide for the future in the management of these cases.

CLASSIFICATION OF PATIENTS

There is a great deal of confusion in the literature on diabetic gangrene because of the failure to classify the cases into comparable groups in which all circumstances are uniform. This is a primary necessity for study; otherwise, statistics are meaningless. The factors that were considered important to determine in each case were the age and general condition of the patient, the duration, severity, and control of the diabetes, the state of the systemic circulation, the type and virulence of the infecting organism, the extent of spread of the infection and its local and general effect upon the patient, the cause, duration, site, type, and extent of the local lesion, and, most important, the degree of circulatory damage.

When these data were recorded and studied, it was found that the extent and virulence of the infection and the degree of circulatory damage were the two which most obviously influenced the course and the result. The others entered into consideration less often than was anticipated.

The cases were divided into those with a normal, good, fair, and poor circulation. Those placed in the group of poor circulation had a severely damaged and often hopelessly inadequate circulation in the feet. They had symptoms of claudication and rest pain, a cold, discolored, pulseless

*This was aided, in part, by the Slevyer's Fund for vascular research.
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foot, trophic changes of skin and nails, absence of a pulse in the popliteal artery, extreme calcification of the vessels in the roentgenogram, and little or no rise in temperature with the vasomotor test. The patients considered to have a fair circulation had moderately severe but not hopeless damage to their arterial circulation. They were in an intermediate position between those with slight impairment and those with severe damage. They gave a past history of claudication but no rest pain. There were moderate temperature, color, and trophic changes in the feet. The dorsalis pedis and posterior tibial arteries had lost their pulsation, but it remained in the popliteal artery. The vasomotor test showed only a moderate rise in temperature with vasoconstriction release. Those placed in the group with a good circulation had a competent blood supply to the feet, but showed evidence of arterial damage, such as symptoms of coldness or numbness, calcification of the vessels in the roentgenogram, or slight temperature and color changes. There was always a detectable, though diminished, pulse in either the dorsalis pedis or posterior tibial arteries in these cases. Infection was usually the indication for admission to the hospital since gangrene was only present in sixteen of the sixty-nine cases. There were twenty-one patients in this series who had no detectable damage to the arteries of their feet, either by physical examination, roentgenographic study, or laboratory tests. They were considered to have a normal circulation. Gangrene caused by infection was present in five cases.

Any division into separate categories has the disadvantage of sharply dividing the cases into groups, whereas actually there are gradual gradations of change. There is no way of quantitatively estimating the percentage of circulatory deficit and, therefore, no way to state specifically how much damage has been done.

ANALYSIS OF RESULTS

General.—There were 211 diabetic patients in the group studied who were admitted to the hospital with infected, pregangrenous, or gangrenous lesions of the feet. They created 277 case records, since some had individual or bilateral lesions which required a separate hospital admission. This was considered a distinct case for study, since it presented its own problem. Of these cases, 102 had poor, 85 had fair, 69 had good, and 21 had excellent (or normal) circulation. This, in itself, is informative, for it shows that the majority (67 per cent) of those who enter the hospital with lesions of the feet already have a serious circulatory defect. This handicaps conservative treatment from the very beginning.

There were 87 men and 124 women in the group. Their average age was 63 years, with extremes from 43 for the youngest to 89 for the oldest. The largest number were in the sixth decade of life. There were nine patients admitted to the hospital in extremis who died and thirteen who refused treatment and left against advice. These should be eliminated.

If this is done, there remain 255 cases who were admitted to the hospital and treated for infection or gangrene of the feet, with forty-one deaths or a surgical mortality of 16 per cent.

TABLE I
255 CASES OF INFECTION OR GANGRENE IN DIABETIC PATIENTS

| CIRCULATION | TOTAL CASES | LEG AMPUTATION | | | | FOOT OPERATIONS ATTEMPTED | | | | NO OPERATION | |
|-------------|-------------|----------------|------------|-------|---------------|---------------------------|------------|-----------|--------|--------------|------------|
| | | PRE-MARY | SEC-ONDARY | TOTAL | MORTALITY (%) | CASES | % OF GROUP | SUC-CESS | DEATHS | CASES | % OF GROUP |
| Poor | 88 | 50 | 14 | 73% | 28 | 23 | 26 | 7 (30%) | 12 | 15 | 17 |
| Fair | 77 | 18 | 14 | 38% | 39 | 35 | 45 | 19 (54%) | 24 | 24 | 31 |
| Good | 69 | 1 | 9 | 14.5% | 30 | 47 | 68 | 35 (90%) | 3 | 21 | 30 |
| Normal | 21 | 0 | 0 | 0 % | 1 | 17 | 81 | 17 (100%) | 0 | 4 | 19 |

Table I, which gives the results of treatment, demonstrates the importance of the circulatory factor in the management of these cases. It is expected that improvement in the circulation would diminish the number of leg amputations and increase the successful operations upon the foot. But it is surprising to find that the mortality from leg amputation is no less with a good than with a poor circulation. This is explained by the increased incidence of acute infection as an indication for amputation in the cases with a competent blood supply and illustrates the importance of infection in causing death.

It should be noted that sixty-four, or 25 per cent, of the 255 cases in the series were cured by conservative, nonoperative treatment. They had superficial wounds which were occasionally treated by removing scabs, crusts, slough, or parts of the nail, but none had an operation of sufficient magnitude to require an anesthetic. Such lesions should be considered, for they often develop into a serious gangrene. Or, if they cannot be made to heal, a leg amputation is often the only other alternative. The conservative treatment becomes dangerous if the wound or infection from it extends into the deeper structures of the foot. If this occurs, operative intervention is indicated.

OPERATIONS ON THE FOOT

Diabetic patients with an adequate circulation who have infected or gangrenous lesions of the foot should be cured by a well-executed local operation. Table II shows that this is always true in the normal group, but not invariably so in those classed as having a good circulation. Here infection, spreading along fascial planes despite wide drainage, was always the cause of failure. But this is the exception, so the attempt to save the foot should be made, for leg amputation is usually a needless sacrifice.

Patients with an inadequate circulation often fail to heal operative wounds in the foot. The percentage of success is small, and the hospital

TABLE II
OPERATIONS ON THE FOOT

| CIRCULATION | CASES OF FOOT OPERATIONS | PERCENT-AGE OF GROUP | DIED AFTER FOOT OPERATION | SECONDARY LEG AMPUTATION | DIED AFTER LEG AMPUTATION | HEALED FOOT WOUND | DAYS TO HEAL | SUCCESS (%) |
|-------------|--------------------------|----------------------|---------------------------|--------------------------|---------------------------|-------------------|--------------|-------------|
| Poor | 23 | 26 | 2 | 14 (51%) | 5 | 7 | 161 | 30 |
| Fair | 35 | 45 | 2 | 14 (40%) | 4 | 19 | 64 | 54 |
| Good | 47 | 68 | 3 | 9 (19%) | 2 | 35 | 55 | 74 |
| Normal | 17 | 81 | 0 | 0 | 0 | 17 | 22 | 100 |

 TABLE IIA
TOE AMPUTATION

| CIRCULATION | CASES OF TOE AMPUTATION | PERCENT-AGE OF GROUP | DIED AFTER TOE AMPUTATION | SECONDARY LEG AMPUTATION | DIED AFTER LEG AMPUTATION | HEALED FOOT WOUND | DAYS TO HEAL | SUCCESS (%) |
|-------------|-------------------------|----------------------|---------------------------|--------------------------|---------------------------|-------------------|--------------|-------------|
| Poor | 17 | 20 | 1 | 12 (71%) | 3 | 4 | 126 | 23 |
| Fair | 29 | 39 | 2 | 13 (45%) | 3 | 14 | 93 | 48 |
| Good | 34 | 50 | 3 | 6 (18%) | 1 | 25 | 62 | 73 |
| Normal | 7 | 33 | 0 | 0 | 0 | 7 | 23 | 100 |

 TABLE IIB
PLANTAR ABSCESS

| CIRCULATION | CASES OF PLANTAR ABSCESS | PERCENT-AGE OF GROUP | DIED AFTER INCISION | LEG AMPUTATION | DIED AFTER LEG AMPUTATION | HEALED FOOT WOUND | DAYS TO HEAL | SUCCESS (%) |
|-------------|--------------------------|----------------------|---------------------|----------------|---------------------------|-------------------|--------------|-------------|
| Poor | 18 | 20 | 0 | 16 (89%) | 6 | 2 | 270 | 11 |
| Fair | 19 | 24 | 1 | 15 (79%) | 6 | 3 | 180 | 16 |
| Good | 24 | 35 | 2 | 9 (37%) | 2 | 13 | 63 | 54 |
| Normal | 3 | 14 | 0 | 0 | 0 | 3 | 36 | 100 |

stay is long. It is important to determine if harm comes from the unsuccessful attempts at foot surgery. It was found that the mortality after toe amputation was 11 per cent; of leg amputation after foot operation, 26 per cent; and of primary leg amputation, 32 per cent. This would indicate a diminished risk after attempted local operation. Moreover, multiple operations on the foot did not increase the mortality rate or diminish the chance of healing; they only prolonged the hospital stay. The real hazard of attempted foot surgery was the introduction of suppuration into the plantar space. This important possibility should be kept in mind when considering an operation on an uninfected foot in a patient with an inadequate circulation. The prospect of success is small and the risk of introducing infection is great, and, therefore, it is best to avoid local surgery.

Plantar abscess was separated in Table IIB for special consideration since it was often a troublesome lesion. It is apparent that, in the poor and fair circulatory groups, the treatment by local incision gives poor results and causes long hospitalization. It is not a satisfactory method of therapy. But it is also seen that the mortality of leg amputation is high, being nearly 40 per cent. This may be subdivided into thirty-two cases treated by primary amputation, with a mortality of 31 per cent, and eight cases treated by secondary amputation, with a mortality of 50 per cent. So, a patient with an inadequate circulation who develops a plantar abscess faces a grave situation which cannot be treated satisfactorily by either local incision or leg amputation. The only other alternative is a two-stage operation with excision of the infected part, followed by leg amputation at a later date.

Cases with an adequate (good or normal) circulation respond more satisfactorily to incision and drainage of a plantar abscess. All of those with a normal circulation and over one-half of those with a good circulation were cured by operations upon the foot.

The impression was gained that one could persist too long in doing multiple operations on these cases. The best results are obtained from wide drainage secured at the first operation. If small secondary pockets occur, they may be opened, but if there is a steady progression of the infection, the prospect of success is slight. Suppuration which extended into the calf was never healed by incision and drainage although this was often attempted.

LEG AMPUTATION

Loss of a limb constitutes a serious threat to the life of a diabetic patient. Our mortality rate from leg amputation was 32 per cent. This was too high and led to an evaluation of the factors that might influence the result. We could find no consistent influence from age, sex, or severity of the diabetes. The competence of the circulation made no difference, for it is seen in Table I that the mortality rate for leg am-

putation in the poor circulatory group is 28 per cent, in the fair group, 39 per cent, and in the good group, 30 per cent. If these figures are correlated with the incidence of infection, it is found that 60 per cent of the poor, 72 per cent of the fair, and 100 per cent of the good circulatory group had acute infection at the time of amputation. This led us to regroup our cases in relation to the presence or absence of acute infection. Fever above 38° C., spreading cellulitis, lymphangitis or pus in the plantar space were considered to be indications of acute infection. Patients with chronically infected lesions were placed in the same group as those who had no infection. It was found that primary leg amputation done in cases *with acute infection* in the foot had a 45 per cent mortality. Primary leg amputation *without acute infection* in the foot had a 12 per cent mortality. In addition, of those with acute infection that survived, 80 per cent had infection of the stump in contrast to 23 per cent in the noninfected group. Because of this, the hospital stay was prolonged.

The type of organism causing the infection did not seem to influence the result, except that *Bacillus welchii* infections were always serious. Delay of the primary amputation with preoperative treatment did not alter either the mortality rate or the incidence infection of the stump. The majority of our cases had closure of the wound of amputation. In those in which the wound was left open, the mortality rate was the same, for, in both, uninvolved fascial planes and devitalized muscle were exposed to infection.

We found that patients having a secondary leg amputation because of failure of operations on the foot had a mortality rate of 26 per cent. This would indicate that local surgical treatment reduces the risk. But the ideal to be achieved is the reduction to the 12 per cent mortality of those who have no acute infection, for this death rate is due to hazards common to any major operation in these patients. This can be done if the acute infection in the foot is eliminated before the leg is amputated. Zierold¹ has stated this principle and has practiced it by removing all infected or devitalized tissue from the foot. After the patient's temperature had remained at a normal level for three days, leg amputation was done as an elective procedure. Zierold reports a reduction in mortality from 50 to 10 per cent by this procedure. McKittrick² and others advocate guillotine amputation in the calf under these circumstances, but McKittrick reports a 35 per cent mortality for his guillotine amputations even though he has attained the excellent result of a 13.9 per cent mortality for all of his major amputations.

Recently, to avoid cutting through muscle, we have tried removing the infected foot by the atraumatic method of disarticulation at the subastragaloid or ankle joint. Later, after the infection has subsided, leg amputation is done at a higher level.

CONCLUSIONS

1. Adequate treatment of gangrene in diabetes requires evaluation of the factors of circulation and infection, for upon these rests the type of therapy and the result.

2. Conservative nonoperative treatment of *superficial* lesions is proper in all degrees of circulatory damage so long as the lesion or infection does not extend into the foot. This course is justified by a cure of 25 per cent of our cases by this method. There is often no alternative but leg amputation.

3. Conservative operative treatment on the foot is indicated in cases with an adequate circulation (good or normal). Leg amputation is usually a needless sacrifice. We obtained 90 per cent cures by operations on the foot in these cases. The failure of the first operation does not increase the mortality or reduce the prospect of success of subsequent procedures; it only prolongs the hospital stay.

4. Patients with an inadequate circulation (fair or poor) who have ischemic gangrene should not be treated conservatively, for delay or local operations may permit infection of the foot. A primary leg amputation is indicated.

5. Patients with inadequate circulation who have infection in the foot may be treated by local operation without increased risk, but the results are poor, for few heal the wound even after a prolonged hospital stay.

6. Patients with acute infection in the foot should never have a primary leg amputation, for the mortality rate was 45 per cent in our series. In contrast, patients without acute infection had a 12 per cent mortality from leg amputation. We believe that patients with an inadequate circulation who have an acute infection are best treated by removal of the infected foot, followed by leg amputation at a later date.

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GASTRIC RESECTION WITH REMOVAL OF THE FUNDUS IN THE TREATMENT OF DUODENAL ULCER

ROBERT ZOLLINGER, M.D., BOSTON, MASS.

(From the Surgical Clinic of the Peter Bent Brigham Hospital and the Department of Surgery of the Harvard Medical School)

THE modern medical treatment of duodenal ulcer is so effective that only the exceptional case requires surgical therapy. In contrast with the situation twenty years ago, when over 50 per cent of such patients came to surgery, now not more than 8 to 10 per cent require surgical treatment.¹⁶ For the treatment of these patients there is a wide choice of operations available to the surgeon. It is not the purpose of this paper to enter into a discussion of conservative versus radical surgery in the treatment of duodenal ulcer but rather to discuss a procedure which aims at a reduction in the total amount of hydrochloric acid secreted.

We have two reasons for utilizing fundusectomy. First, we have been dissatisfied with the results obtained by some of the other accepted methods of resection. In the surgical management of duodenal ulcer in the Peter Bent Brigham Hospital we have attempted to follow the physiologic implications laid down as the result of experimentation on this problem. In our opinion the Horsley modification of the Billroth I type of operation seemed to answer best the experimental requirements. It provides for resection of the ulcer-bearing area and reanastomosis of the remaining stomach to the duodenum, which has a higher tissue resistance to gastric juice than the jejunum; it gives a patulous pylorus, so essential in avoiding recurrent ulceration from a mechanical cause; and, in addition, it permits a certain amount of intragastric regurgitation of alkaline duodenal juices. But after clinical trial, when approximately 50 per cent of the cases followed for five years developed recurrent difficulty, it was abandoned.

From clinical and experimental evidence repeatedly presented, the important role played by the acid factor in the etiology of duodenal and gastrojejunal ulceration must be acknowledged. The weakness of Billroth II types of resection is that sufficient acid-bearing tissue is not removed. Even in so-called radical resection of the Billroth II type, when three-quarters or more of the stomach is removed, it is customary to carry the resection high on the lesser curvature and to leave a sufficient amount of greater curvature to facilitate gastrojejunal anastomosis. Apparently fear of a gastric ulcer developing in this location after resection prompts this wide removal of lesser curvature. Clinically, however, recurrent ulceration occurs almost invariably in the jejunum

¹⁶Presented at the meeting of the Society of University Surgeons at New York, N. Y., February 9 and 10, 1940.

or about the stoma and is uncommon on the lesser curvature after resection for duodenal ulcer. It is also infrequent after gastroenterostomy, as shown by Ginzburg and Mage. They found, in a study of 86 specimens resected because of the failure of posterior gastroenterostomy, that lesser curvature ulcers developed in only six instances. In each case posterior gastroenterostomy had been performed originally for duodenal ulcer. Not only do marginal or jejunal ulcers occur after conservative surgical procedures, but they are not infrequent after the Billroth II types of resection.¹⁰ A five-year follow-up, including roentgenologic examination, of a group of selected cases of intractable duodenal ulcer having had resection would probably show a distressingly high percentage with recurrent difficulties. The incidence of recurrent ulceration after resection may be partially explained by the fact that various amounts of fundus, rich in surface area of acid-secreting tissue, have been retained, although most of the lesser curvature, low in surface area of acid-secreting tissue, has been resected.

Second, the clinical results and experimental evidence imply that fundusectomy is sound. A number of years ago Connell^{3, 4} proposed diminishing the hydrochloric acid secretion in patients with intractable duodenal ulcer by means of partial fundusectomy. He has since reported satisfactory results with the use of this procedure in the treatment of complicated jejunal ulcerations as well.⁶

Accumulated experimental evidence, however, has perhaps retarded the widespread use of fundusectomy, since it has been repeatedly demonstrated that the acid value by gastric analysis returns to normal within a period of a few months, depending upon the amount of fundus removed.^{8, 12, 14, 15} As Mann⁵ and others have pointed out, however, if permanent clinical results are to follow fundusectomy, it must be on the basis of actual reduction of the amount of gastric juice and not of any change in the degree of acidity as shown by gastric analysis.

That the volume of acid secreted is markedly decreased may be assumed from comparing a cross section of the stomach of a normal dog with that of one in which the fundus has been resected (Fig. 1). In dogs, despite removal of a large amount of the fundus, the stomach eventually returns to approximately normal size and capacity. The effect of removal of the fundus can more easily be appreciated after fixation and sectioning of the stomachs at corresponding levels. Normally, the region of the fundus along the greater curvature presents a great duplication of thick folds, providing a large surface area of acid-secreting tissue, but after fundusectomy a section at a corresponding level shows an absence of folds. Although the acid values by gastric analysis would appear the same, the volume of acid secreted would obviously be tremendously decreased in the second specimen. After fundusectomy the alkaline juices would be sufficient to combat the decreased volume of gastric juice, thereby preventing recurrent ulceration. Confirmation of this is suggested by the investigations of Fauley and

Ivy, who performed fundusectomy in animals and followed it subsequently by the Mann-Williamson operation. They found that, although the free acid and total acid values returned to normal within a period of six to eight months, the quantity of gastric juice that could be aspirated in response to injection of histamine was substantially less than in nonfundusectomized Mann-Williamson dogs and slightly less than in normal control animals. Furthermore, they found that fundusectomy, combined with an easily assimilable diet, protected the Mann-Williamson animals against ulceration for the two years during which the animals were observed. This protection was not universally effective without the special diet, but it seemed to indicate a decrease in the quantity of acid available for prolonged irritation of the jejunum. Not only do the experiments of Fauley and Ivy indicate the possible usefulness of fundusectomy in the treatment of jejunal ulcer, but they serve to emphasize the need for a strict dietary regimen in patients after operation.



Fig. 1.—A, A transverse block taken through the midfundus of stomach of a normal dog. Note smooth *magenstrasse* of inner curvature and the immense reduplication of mucous membrane over greater curvature. B, Transverse block through the midfundus of stomach of a dog after fundusectomy. Rugae are almost totally lacking. (From Seeley and Zollinger: *Courtesy of Surg. Gynec. & Obst.* 61: 155-161, 1935.)

After weighing the experimental and clinical evidence for fundusectomy, we carried out, in addition to resection of the stomach by the Polya method, a removal of varying amounts of the fundus (Fig. 2). Resection of the antrum, especially in severe cases of jejunal ulceration after gastroenterostomy, seemed desirable in the belief not so much that it would reduce the secretory capacity of the stomach as that it would provide a patulous stoma. In addition to fundusectomy a departure from the radical type of Polya resection was decided upon, in that the lesser curvature was not to be divided high but in the neighborhood of

the incisura angularis. This would insure a longer tube of stomach along the lesser curvature, would provide a more satisfactory postoperative gastric capacity, and would facilitate gastrojejunal anastomosis. The anastomosis could be easily carried out in the immediate field of operation with adequate room and exposure for the meticulous technical steps associated with closure of the upper and lower angles of the stoma. The obvious difficulty that suggested itself was the danger associated with the approximation of two suture lines at the lower end of the gastrojejunal anastomosis especially, when the blood supply of the remaining stomach would be dependent only on the left gastric artery (Fig. 2). Injection of the left gastric artery in a stomach removed at post mortem, using a mixture utilized by Schlesinger, clearly demonstrated the rich blood supplied by the left gastric artery (Fig. 3). Although the blood supply could be shown to be adequate, even in the region where the two suture lines would be approximated, the technical details of such a procedure were first tested experimentally in animals. Since we carried out these experiments, Wangenstein has reported extensive removal of the acid-bearing tissue, including the fundus. He did not hesitate to do a gastroenterostomy at various levels along the suture line and had no difficulty from impaired blood supply.

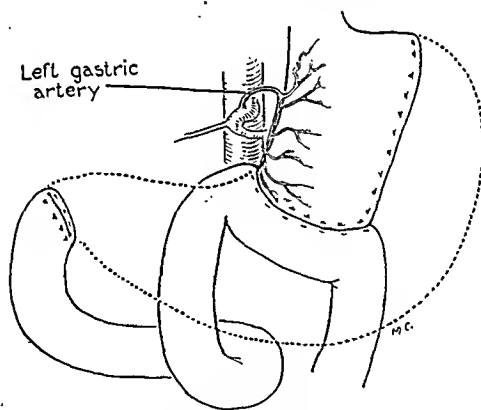


Fig. 2.—Schematic drawing, illustrating Polya resection combined with fundusectomy. Note the amount of lesser curvature retained.

The following experiments were carried out. The lesser curvature was divided between medium-sized Payr clamps about the incisura angularis in the majority of instances. The fundus was then resected, leaving only a narrow tube along the lesser curvature (Fig. 2). Following resection, an anastomosis was made between the open end of the stomach and the upper jejunum. It was found that the blood supply was adequate and that approximation of the two suture lines at the lower angle of the anastomosis could be carried out with safety. Results were the same whether the proximal jejunum was anastomosed to the lesser or to the greater curvature. Four dogs survived this procedure and were allowed to live from six to thirteen months.

At the time of sacrifice, none of the animals showed evidence of jejunal ulceration. In the first animal the lesser curvature was divided so high that only a short tube of stomach remained. In spite of hypertrophy of the gastric remnant, the stomach was apparently insufficient. The animal could retain little food and was emaciated when sacrificed thirteen months after operation. The remaining three animals, in which the lesser curvature had been divided about the incisura angularis, remained in excellent condition and showed no essential variation in weight. There was considerable hypertrophy and dilatation of the stomach at the time of sacrifice (Fig. 4). Injection of the left gastric artery demonstrated a liberal and adequate blood supply to the stomach (Fig. 4). Gastric analyses were not carried out in these animals because experimental data have been accumulated to indicate that the gastric analyses had returned to normal by the time of sacrifice. The volume of acid secreted, however, must have been materially decreased.

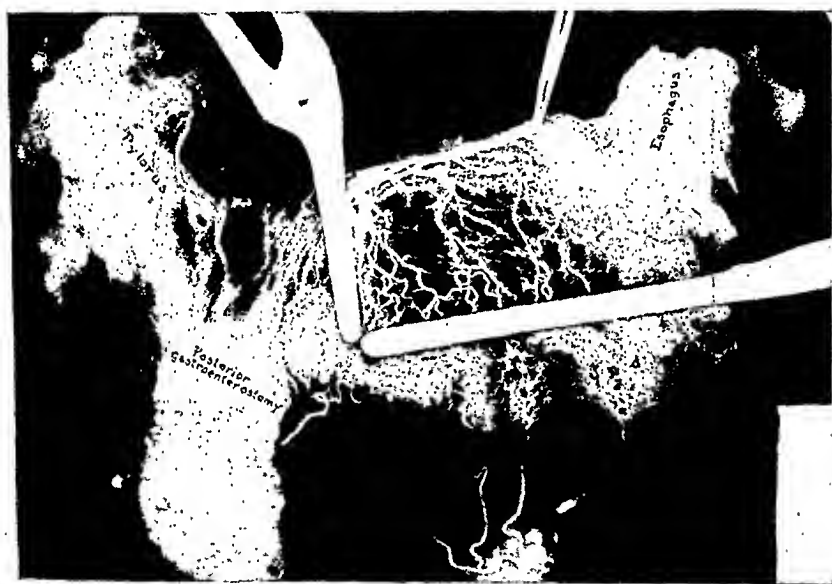


Fig. 3.—Injection of opaque material into left gastric artery of post-mortem specimen, illustrating the adequacy of the blood supply. Payr clamps outline the amount of stomach retained.

Before attempting fundusectomy, the surgeon should be familiar with the extent and distribution of the acid-secreting cells of the stomach to insure removal of a sufficient amount of acid-bearing tissue. Berger's study shows that there is a zone in the region of the cardia where the ratio of acid-bearing cells is about 50 per cent. This is in contrast to 100 per cent for a large area extending from the cardia down to the region of the incisura angularis and over to the junction of the body and antrum. He found a limited transition zone in the region of the incisura angularis where the incidence of acid-bearing cells is 75 per cent. In view of the large folds of mucosa along the greater curvature

in the region of the body and fundus it is obvious that here is a chief area of acid-secreting tissue. This is shown schematically by the wavy lines in the drawing in the 100 per cent zone of parietal cells (Fig. 5). In order that sufficient acid-bearing tissue may be removed, the resection must extend well up toward the esophagus along the greater curvature.

Gastric resection with removal of a large amount of the acid-bearing tissue by means of fundusectomy and with restoration of gastric con-

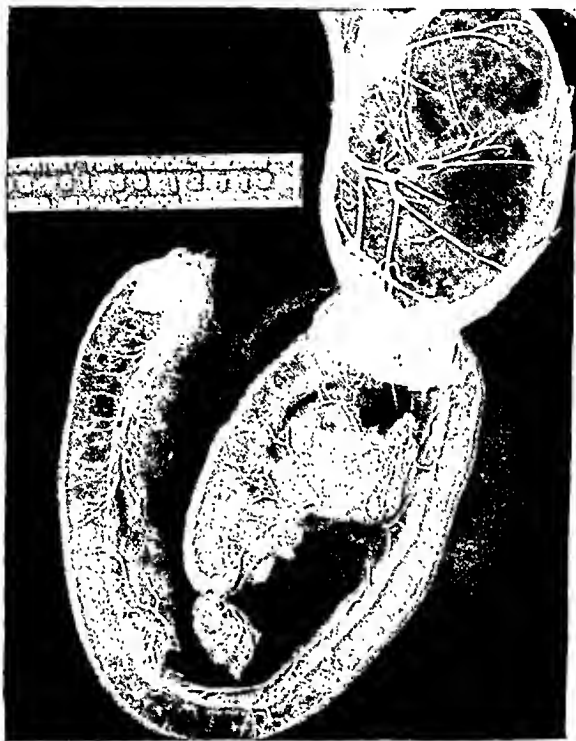


Fig. 4.—Injected specimen of stomach of a dog six months after resection with fundusectomy. The left gastric artery has been injected with opaque material. The stomach has satisfactory capacity.

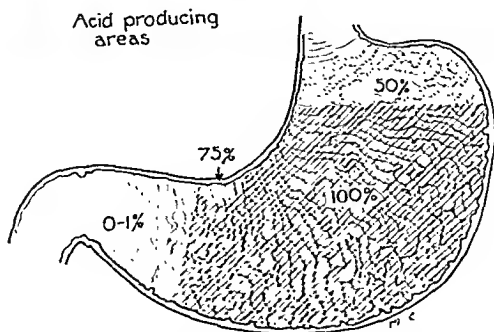


Fig. 5.—Schematic drawing of acid-bearing area, illustrating the reduplication of folds along the greater curvature and the percentage of acid-bearing cells at various levels (Berger).

tinuity by a gastrojejunostomy of the Polya type to a long tube of lesser curvature has been performed in the following manner on two patients: Under ether anesthesia the abdomen was opened through a high, left, paramedian incision. After the ligation of the blood supply to the region of the pylorus, the pylorus was divided and the duodenum was closed. The blood supply of the lesser curvature was then carefully ligated up to the incisura angularis. The blood supply of the greater curvature was next ligated high on the fundus, unless adhesions between the stomach and spleen interfered (Fig. 6). As Wangenstein has pointed out, it may be difficult to mobilize the fundus entirely because of a short gastrosplenic omentum. Usually, however, this is not a particularly difficult problem. The left gastric artery now remained as

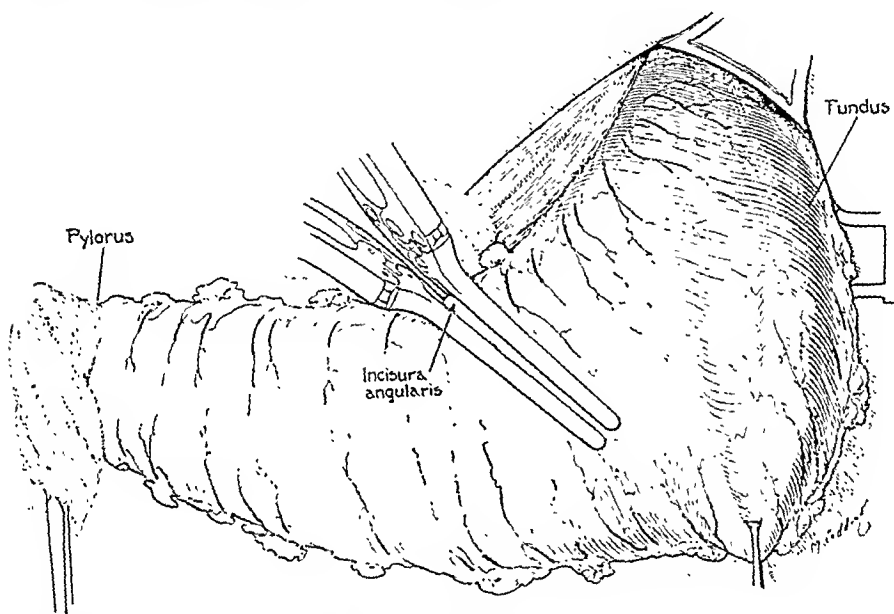


Fig. 6.—The duodenum has been divided and closed. The blood supply of the stomach has been divided to the incisura angularis and high on the fundus. Medium-sized Payr clamps are applied at the incisura angularis in preparation for division of the lesser curvature.

the source of the blood supply. An area on the lesser curvature about the incisura angularis and one high on the fundus at a selected level were freed of fat in preparation for the application of clamps. A pair of medium-sized Payr clamps of sufficient size to permit the subsequent stoma to admit approximately three fingers were applied at the point prepared on the lesser curvature (Fig. 6). The tissue between the clamps was divided with the cautery and the Payr clamp toward the pylorus was reflected downward (Fig. 7). Two long Payr clamps were applied close to the tip of the remaining Payr clamp and as high on the fundus as it had been prepared (Fig. 7). As the first large clamp is applied, the surgeon should assure himself that the stomach is not rotated and that sufficient stomach remains so that, when the contents of the large Payr clamp are sutured and inverted, there is a satisfactory

lumen of the stomach along the lesser curvature. The use of a DePetz sewing clamp, as advocated by Wangensteen, should facilitate the closure of the newly made greater curvature. A cautery was again used to divide the contents of the large Payr clamps. A running, continuous silk suture on a milliner's needle was started near the toe of the clamp and was passed beneath the clamp to approximate the gastric walls and

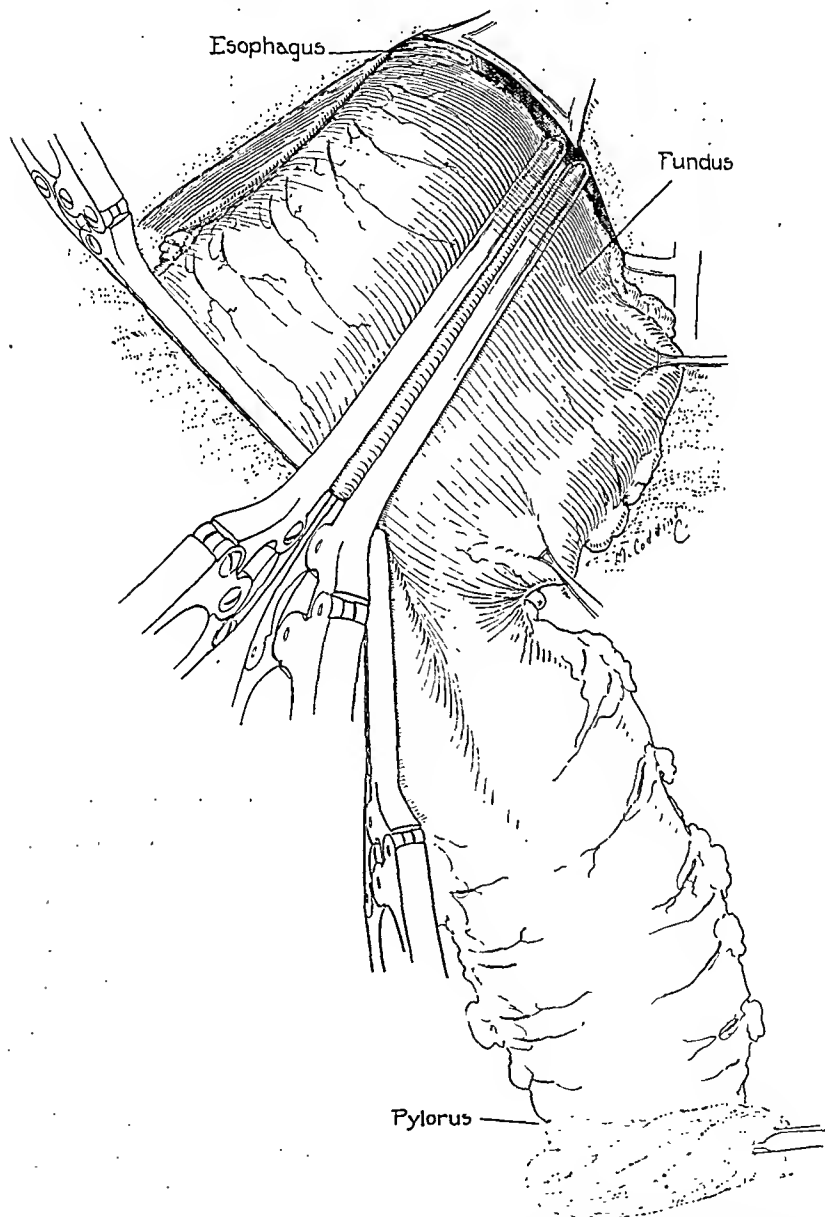


FIG. 7.—The lesser curvature has been divided. A pair of large Payr clamps are applied in preparation for resection of the fundus. A sufficient lumen of the stomach along the lesser curvature must be assured before the large clamps are finally locked.

to control the blood supply (Fig. 8). This suture was carried up to the toe of the smaller Payr clamp and tied. The crushed contents of the large Payr clamp may be excised and additional sutures taken, if necessary, to approximate more accurately the cut margin of the gastric wall and to control any bleeding points. This suture line was buried by a second layer of interrupted sutures of the Halsted mattress type (Fig. 9). These interrupted sutures were also carried up to the small Payr clamp.

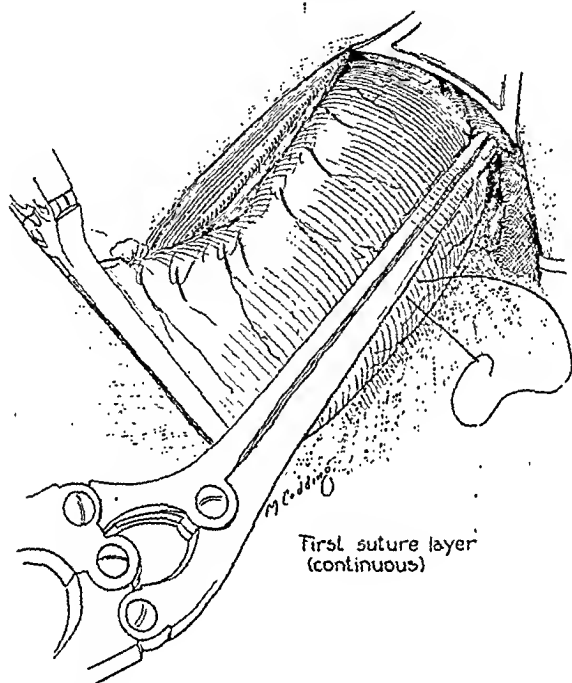
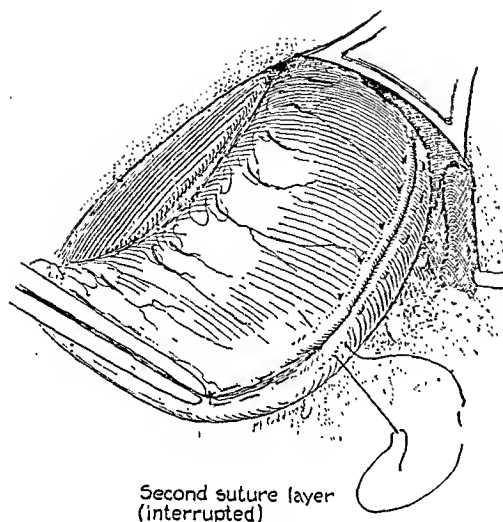


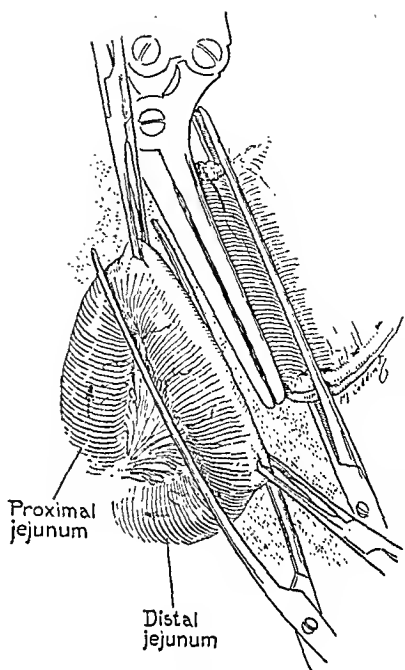
Fig. 8.—The contents of the large Payr clamp are approximated with a continuous silk suture. The crushed contents of the clamp are excised.

Each of the two patients in whom this operation was carried out had had a previous gastroenterostomy with a resultant jejunal ulcer, so that it was necessary to close the opening in the jejunum and to select a site distal to the ulcerated area for the new gastrojejunal stoma. A routine gastrojejunal anastomosis of the Polya type was performed (Fig. 10). By dividing the stomach low on the lesser curvature, the gastrojejunal anastomosis can be done in the immediate operative field. There has been no particular difficulty experienced in closing the inferior angle of the stoma where it meets the suture line of the fundusectomy. The jejunum, however, should preferably be anchored with interrupted Halsted sutures slightly up over the lesser curvature and for a short distance at the inferior angle to avoid tension on the initial sutures about the angles of the anastomosis (Fig. 11). The mesocolon was then anchored up above the gastrojejunal anastomosis. In both of the patients in whom this technique was followed a stoma which would admit three fingers was obtained.



Second suture layer
(interrupted)

Fig. 9.



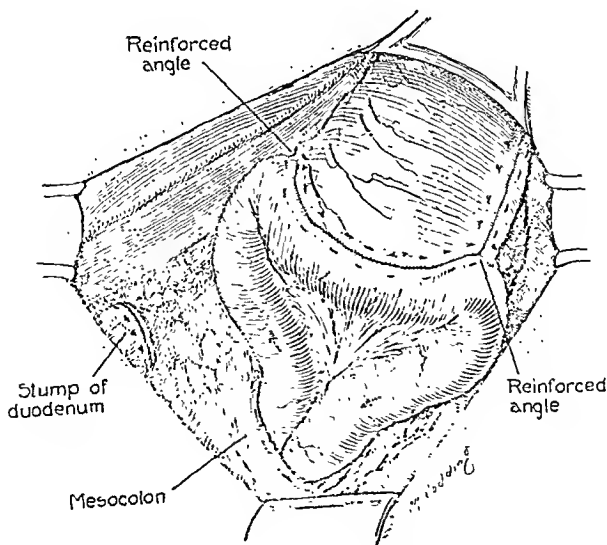
Proximal
jejunum

Distal
jejunum

Fig. 10.

Fig. 9.—A final serosal layer of interrupted silk mattress sutures is taken to cover the initial suture line.

Fig. 10.—The jejunum is anastomosed to the entire open end of the stomach. The stoma should admit approximately three fingers.



Reinforced
angle

Stump of
duodenum

Mesocolon

Reinforced
angle

Fig. 11.—The angles of the gastrojejunal anastomosis are reinforced with several additional interrupted silk sutures. The mesocolon is anchored to the stomach above the anastomosis.

ZOLLINGER: TREATMENT OF DUODENAL ULCER

The two patients selected for this procedure had jejunal ulceration after posterior gastroenterostomy for duodenal ulcer. Their symptoms were not relieved by hospitalization and adequate medical treatment.

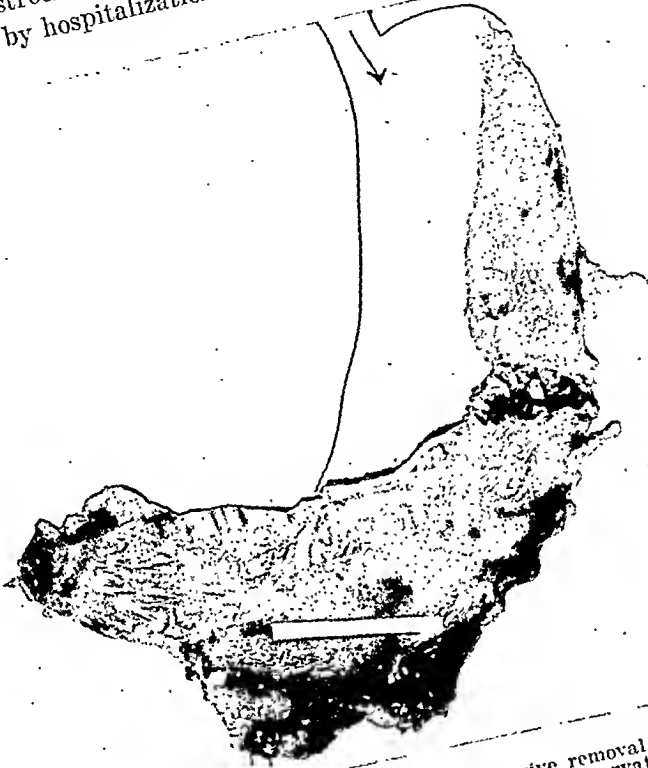


FIG. 12.—A specimen of Case 1, illustrating the extensive removal of fundus and the amount of stomach retained along the lesser curvature.

REPORT OF CASES

CASE 1.—A 43-year-old Jewish bartender had ulcer symptoms intermittently over a period of twenty-five years. In 1921 a posterior gastroenterostomy was performed elsewhere with relief of symptoms for six months. In 1923 another gastric operation was performed, the details of which are lacking. Following the second gastric operation the patient was free of symptoms for approximately ten years. However, for six years prior to his entry on the Medical Service of the Peter Bent Brigham Hospital, May 12, 1939, he had recurrent symptoms which gradually increased in severity. He had a proved jejunal ulcer which failed to respond to medical treatment. He was kept on a strict Sippy regimen for thirty-five days with a constant creamlin drip for six days. Because of continued distress, he was given eight roentgen-ray treatments in an effort to reduce the gastric acidity. He was then discharged from the hospital. He gained ten pounds in weight. Although he improved after the x-ray therapy, he was not completely relieved of his symptoms and accordingly he entered the Surgical Service on July 21, 1939. A gastric analysis on the Medical Service had shown free acid of 65 and a total acid as high as 92, but following the x-ray therapy the acid values by gastric analysis were substantially decreased. On July 26, 1939, an exploratory operation was performed. This showed a healed duodenal ulcer and a jejunal ulcer. The operation previously described was performed with closure of the jejunum at the site of the ulcer. A point was selected

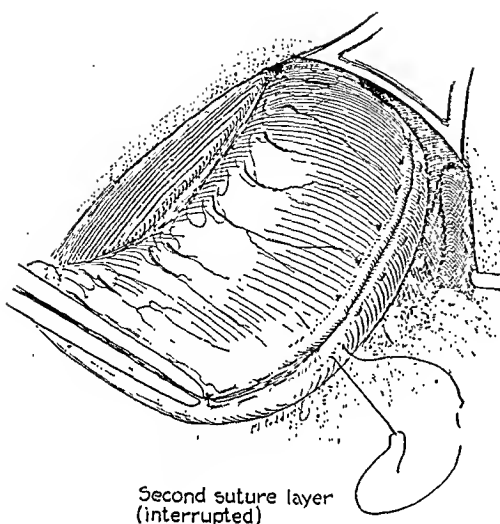


Fig. 9.

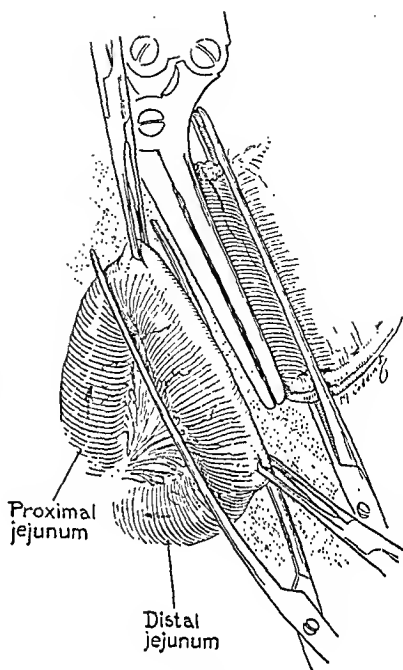


Fig. 10.

Fig. 9.—A final serosal layer of interrupted silk mattress sutures is taken to cover the initial suture line.

Fig. 10.—The jejunum is anastomosed to the entire open end of the stomach. The stoma should admit approximately three fingers.

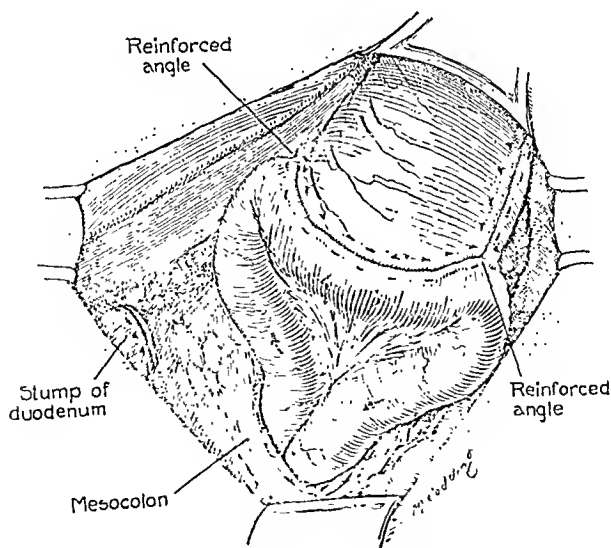


Fig. 11.—The angles of the gastrojejunostomy are reinforced with several additional interrupted interrupted silk sutures. The mesocolon is anchored to the stomach above the anastomosis.

missions were for pain associated with jejunal ulcer, and one was for a severe hemorrhage with a fall in the red blood count to two million. He has had previous tarry stools and on various occasions had vomited coffee-ground material. A jejunal ulcer was proved by x-ray in 1930 and by subsequent examinations. During two weeks of treatment on the Medical Service he showed only partial improvement. It was felt that he was a severe case which required radical resection. Gastric analysis,

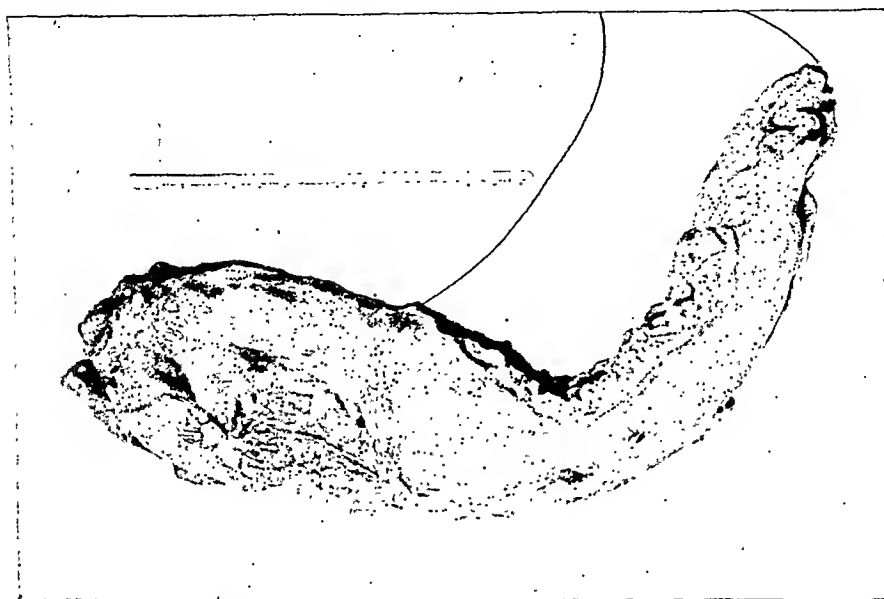


Fig. 14.—Specimen of Case 2, showing the amount of stomach resected.

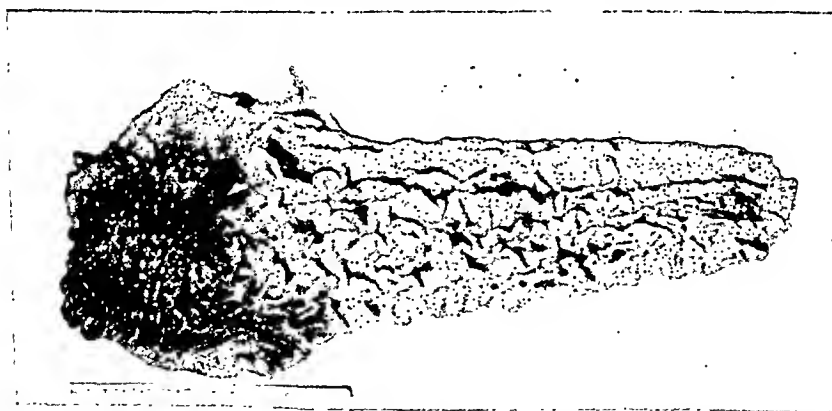


Fig. 15.—Specimen of Case 2 opened, showing the small stoma of the previous gastroenterostomy as well as the large folds of acid-bearing tissue removed by fundusectomy.

from time to time, showed a free acid as high as 70, which went as high as 105 after histamine. As much as 150 c.c. of acid could be aspirated after histamine. On Dec. 20, 1939, a radical resection with fundusectomy was carried out. In this patient the resection was not carried quite as high on the fundus as described in Case 1. However, the stomach was large so that the resected specimen measured 37 cm. along the greater curvature (Fig. 14). The specimen, when opened, showed that the resection had apparently been carried high enough on the greater curvature to extend above the large rugae (Fig. 15). At that time a jejunal ulcer was found, and the

for the anastomosis about 12 cm. distal. The specimen measured 30 cm. along the greater curvature; 1.5 cm. of duodenum were included in this resection (Fig. 12).

The patient had an uneventful postoperative course. He occasionally vomited a small amount of bile, especially at night, but otherwise all symptoms were relieved. His economic situation, which did not permit an adequate diet, was thought to be responsible for this complaint. Accordingly he was brought back to the hospital for regulation of his diet and for further investigation. He now has work which provides a living wage and has since been symptom free. It is six months since his operation was performed. X-ray examination six months after operation showed a tubular stomach, 8 cm. in length and 6 cm. wide (Fig. 13). The stomach emptied rapidly and there was no evidence of tenderness or crater about the stoma. At the time of operation, silver clips (Cushing) were placed along the greater curvature, about the stoma, and at the site of the previous jejunal ulcer. These, it was hoped, might prove of value in estimating the amount of subsequent hypertrophy and dilatation of the gastric tube at roentgenologic examination.

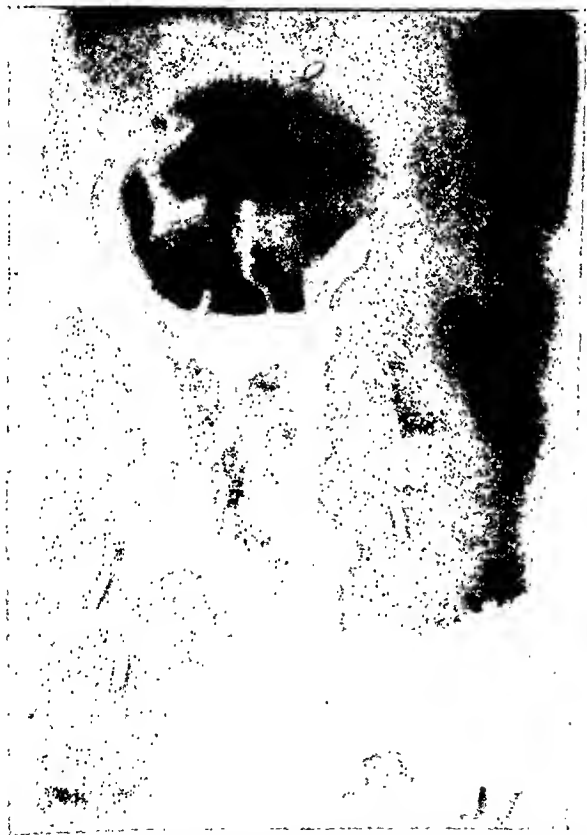


Fig. 13.—Barium study of Case 1, six months after operation, showing a small tube of lesser curvature. The metal clips outline the extent of the fundusectomy and the angles of the gastrojejunal anastomosis.

CASE 2.—A 50-year-old laborer, originally from the British West Indies, entered the Medical Service of the Peter Bent Brigham Hospital, Dec. 8, 1939, for his seventh hospital admission. He complained of severe epigastric distress and anorexia. In 1924 a posterior gastroenterostomy was performed elsewhere for duodenal ulcer with relief of symptoms for two years. Since that time he has been treated in the Out-Patient Department because of recurrent symptoms. Five of his hospital ad-

clusions to be drawn. Such an examination, to be of any value, must be done at least a year after operation. Wangensteen has reported that the patients in whom he has carried out a similar radical excision of the fundus showed no free hydrochloric acid on a fasting stomach after an alcohol test meal, and several months after operation three patients had no free hydrochloric acid even after histamine. The one patient who had symptoms after operation showed free hydrochloric acid on a fasting stomach. In this particular patient the excision of the fundus beyond the insertion of the esophagus was omitted.

Sufficient data are not available yet to determine the actual efficacy of fundusectomy, either with or without short-circuiting procedures or resection. The clinical and experimental reports, however, indicate that removal of the fundus might be considered in the severe case of duodenal ulcer or recurrent ulceration following previous surgical procedures. The final evaluation of any operation for ulcer cannot be determined until a sufficient number of cases has been followed, with roentgenologic examinations, for a period of at least five years.

CONCLUSIONS

Experiences in the use of extensive fundusectomy, combined with the Polya type of resection, in the treatment of jejunal ulcer following gastroenterostomy are reported.

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jejunum was closed at this point. The site for anastomosis was selected about 12 cm. beyond the point of jejunal ulceration. The postoperative course was uneventful.

Postoperative x-rays showed that the remaining portion of the stomach was funnel shaped, measuring 13 cm. in length and 9 cm. in width at the upper end (Fig. 16). Barium emptied rapidly through the stoma. Although the period since operation has been short, this patient has been entirely symptom free and has a gastric capacity greater than the first patient.



Fig. 16.—Barium study of Case 2, one month after operation, showing a larger gastric capacity than Case 1.

The gastric secretion in both patients after operation is consistent with the amount of fundus removed and with experimental findings. It is difficult though to obtain an accurate estimation of the volume response by gastric analysis because the stomach empties so rapidly in these patients. We are not so much interested in the return of acid values, because we expect that these patients may develop a relatively normal gastric analysis. However, these patients will be checked repeatedly for the volume response to histamine by the continuous aspiration method as advocated by Bloomfield and Pollard. Repeated analyses by their careful method should give information as to whether or not there will be a subsequent increase in the volume, which might approach the preoperative analyses. Furthermore, it is realized that neither one of these patients has been studied long enough after operation for definite con-

of their blood supply, taking with them the lymphatic area involved. The mobilization, with freeing of the bowel, is continued to the point selected for transection. Before the bowel is cut, the retroperitoneal space is closed as completely as possible. The case of this closure varies considerably in different patients, but it can be accomplished more readily through the transverse approach mentioned above.¹ At

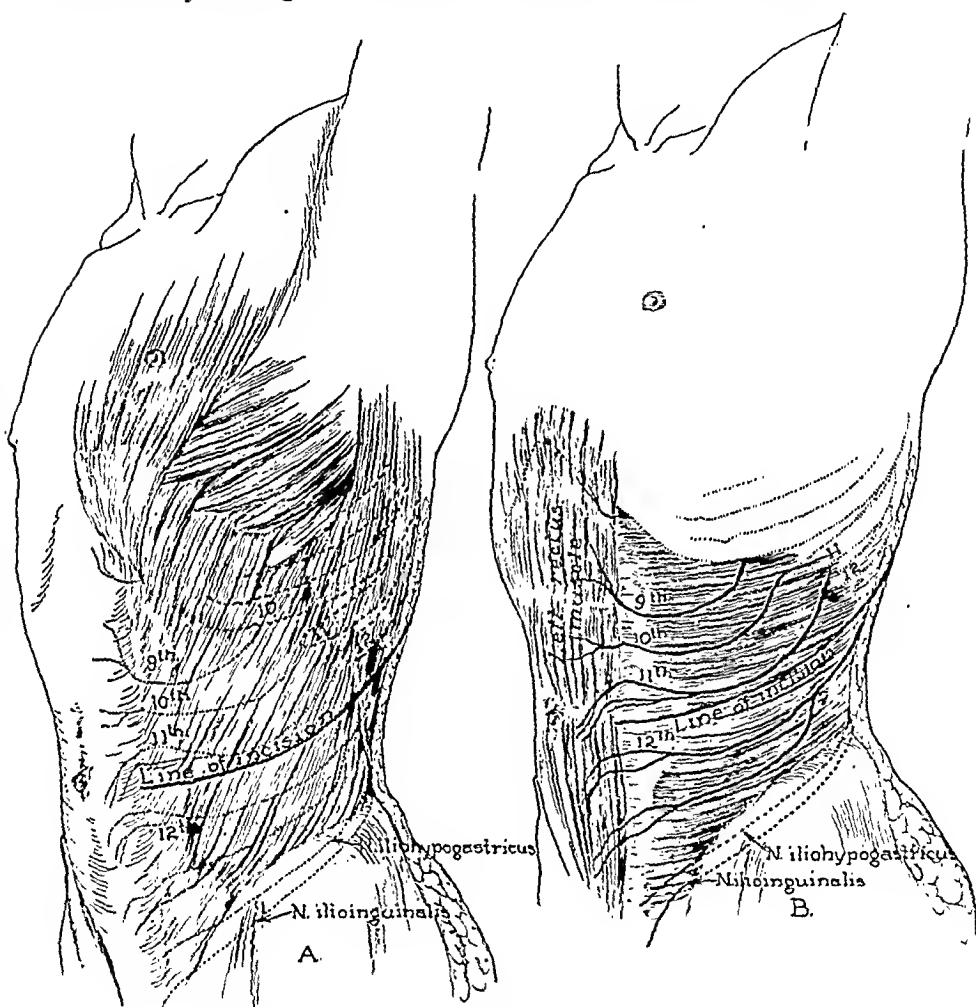


FIG. 1.—Course and distribution of the abdominal nerves. Line of pericostal-trans-abdominal incision between eleventh and twelfth nerves.

this point, the operation can be completed as a Mikulicz procedure, as advocated by many surgeons, if it seems desirable. If the operation is continued, the flow of intestinal contents in the loop to be resected is prevented by the application of a broad rubber band (Fig. 2). We feel that this causes less trauma to the bowel and the blood supply than clamps do. The bowel is transected between clamps by the electro-surgical unit and the ends of the cut bowel are turned in with catgut

RIGHT COLECTOMY IN ONE STAGE

H. GLENN BELL, M.D., AND R. BRUCE HENLEY, M.D.,
SAN FRANCISCO, CALIF.

(From the Department of Surgery, University of California Medical School)

WE HAVE had 27 cases of right colectomy at the University of California Hospital during the last ten years. Though this is far from a large number, we believe that something may be gained by a careful analysis and study of these cases. In addition, 14 patients had lesions for which palliative surgery alone could be done, so that the operability of all lesions of the right colon was 66 per cent.

The subject of the value of right colectomy in one stage as opposed to that in two stages is as controversial now as it was years ago. Each procedure has certain advantages and it certainly is not our idea to recommend, dogmatically, that all patients be operated upon in one stage. As in other types of surgery, patients should be selected carefully for each procedure. In our hands the mortality rate of the two types of operation has been approximately the same. We realize, however, that one additional death in either group would make the mortality reading entirely different.

Advantages of the one-stage operation are that the technical procedure is easier, hospitalization is shorter, thereby reducing the cost of medical care, and only one anesthetic need be administered instead of two. We believe that an earlier recognition of lesions in the right colon, which is the most significant factor influencing the mortality rate, longer preparation before operation, and greater attention to technique will permit more patients to be operated upon by the one-stage procedure, with a lower mortality, than is the case at present.

In the one-stage procedure it is essential that the bowel be clean and decompressed and the body fluids and chemistry be up to normal. The preoperative care should be continued long enough to permit a study of the function of the liver and kidneys, to build up the blood by transfusion, to decompress the bowel by continuous suction through the stomach, and to wash out the lower bowel by the means of enemas and the giving of epsom salts. These procedures are followed by the use of lead and opium pills for two days. This regime, of course, is not applicable if the patient has an acute obstruction.

Adequate exposure is of first importance and we have found the Iliaq¹ incision to be a great improvement over the rectus incision. By its use, mechanical retraction becomes unnecessary, thus lessening trauma to the wound and allowing greater protection to its edges.

The right colon is mobilized in the usual manner by cutting the lateral peritoneum, and the right colon and terminal ileum are freed

¹Presented at the meeting of the Society of University Surgeons at New York, N. Y., February 9 and 10, 1940.

anteriorly and tied. The anastomosis is then covered with omentum. Gloves and drapes are changed again before closure of the abdomen is begun. The abdomen is closed without drainage. Enterostomy proximal to the anastomosis is not performed.

In our series of 27 colectomies, 23 were done for carcinoma, with 3 deaths; 2 were done for tuberculosis, 1 for polyps of the ascending colon and 1 for cicatrizing enteritis, with no deaths. Eight were done in two stages, with 1 death, a mortality of 12.5 per cent; 18 were done in one stage with 2 deaths, a mortality of 11.1 per cent; 1 was done as a Mikulicz procedure, with recovery.

The ages of our patients varied from 30 to 74 years, the largest number being between the ages of 60 and 70 years. There were 14 women and 9 men in the series.

Of the 4 patients with lesions other than carcinoma, none has died. Of the 23 with carcinoma, 14 are still alive (Table I) and 9 have died. Three died following surgery. Of the other 6, 1 lived for two years and four months after operation, 2 lived for thirteen months, 1 for eleven months, 1 for nine months, and 1 for five months; all 6 died of metastases. Of the 3 patients who died after operation, 1, a man 52 years old, had uremia following a complete anuria after the second stage of the operation. No injury to the kidneys or ureters was found at autopsy; the anastomosis was intact. One woman, 61 years of age, died as a result of gangrene of a portion of the small bowel. The tumor was attached to the small bowel and mesentery and apparently the blood supply had been injured to the extent of producing gangrene.

TABLE I

CARCINOMA PATIENTS LIVING AND WELL AFTER RIGHT COLECTOMY

| LESS THAN 1 YR. | 1-2 YR. | 2-3 YR. | 3-4 YR. | 5-6 YR. | 6 YR. | TOTAL |
|--------------------|------------|------------|------------|------------|----------|-------|
| 7 | 2 | 1 | 1 | 2 | 1 | 14 |

In many clinics this resection would not have been attempted. At autopsy the suture line was intact. One man, 47 years of age, died on his seventy-first day after operation from abscess of the right lung and empyema. At autopsy the abdomen appeared to be normal.

SUMMARY

Twenty-seven cases of right colectomy, with three deaths, are reported. Longer preparation before operation and more careful surgical technique will save more of these patients from death by peritonitis. In our opinion, the use of the electrocoagulation unit is an added factor of safety.

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sutures and reinforced with Halsted mattress sutures of silk. During this procedure the wound and abdomen have been packed off carefully so as to prevent the slightest contamination. The ileum and transverse colon are approximated and held in place by traction sutures for a side-to-side anastomosis. We feel that this is the safest anastomosis because the poor blood supply of the transverse colon can thus be supplemented by collateral circulation from the adequate blood supply of the ileum. The abdominal cavity and wound are further isolated by more abdominal packs. The first posterior row of sutures (interrupted silk) is laid, then tied and cut (Fig. 2). The anterior Halsted mattress sutures are laid, retracted over the stay sutures and covered with moistened packs to prevent contamination. The bowel is opened with the electrosurgical unit (Fig. 2) by coagulation and cutting so that there is no bleeding of the cut edges—one of the main sources

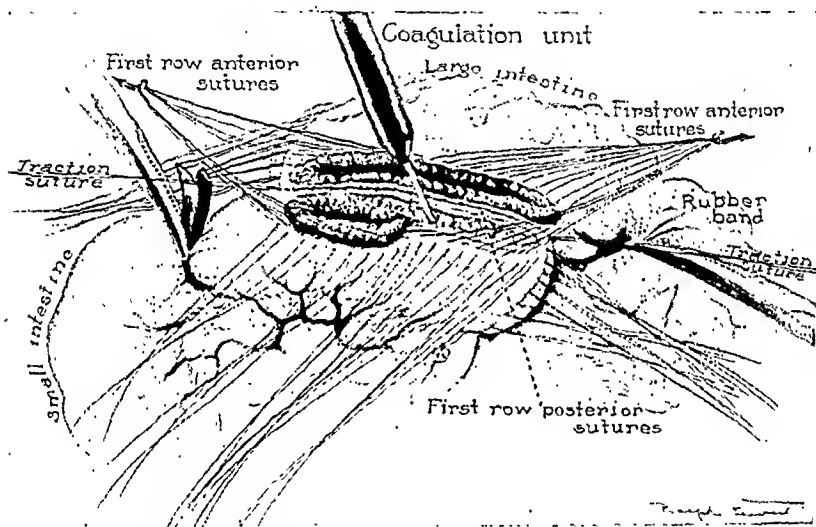


Fig. 2.—Technique of right colectomy. (From Hoag, Carl L.: A New Approach to Resection of Cancer of the Colonic Flexures, California and West Med. 45: 148, 1936.)

both of local contamination of the bowel at the site of anastomosis and of soiling of the abdominal cavity. If the machine is adjusted correctly there should be no free blood on the edges of the wound. The idea of using the electrosurgical unit is not original with us, but it seems to us that this feature has not been emphasized strongly enough.

The second posterior row of sutures (catgut), through the entire posterior layer, is then placed and continued anteriorly to catch just the mucosa and submucosa. This row of sutures is laid entirely with instruments. At this point in the operation, both the superficial packs and the gloves are changed so that another opportunity for contamination is eliminated. At this stage the anterior sutures are drawn tight and tied. A second row of Lembert sutures (silk) is placed

in the skin of experimental animals can be found easily if serial sections are impregnated by the special methods for nerve fibers. Quite recently Josefson¹³ was able to demonstrate minute neuromas in the finger after amputation in three cases and after incised wounds in two cases.

TABLE I
CASES OF PAINFUL SCAR

| CASE* | LOCA-TION | CAUSE | AGE OF SCAR (MO.) | DURA-TION OF PAIN (MO.) | TYPE OF PAIN | MICROSCOPIC FINDINGS | FOL-LOW-UP (MO.) |
|-------|-----------|--------------------|-------------------|-------------------------|-----------------------------|--------------------------|------------------|
| 1 | Foot | Laceration | 30 | 12 | Sharp, spot | Small neuroma | 36 |
| 2 | Breast | Mastectomy | 24 | ? | Two spots | Large neuroma | 7 |
| 3 | Breast | Mastectomy | 17 | 9 | Sharp, spot | Loose neuroma | 0 |
| 4 | Breast | Mastectomy | 36 | ? | Sharp, two spots | Small neuromas | 8 |
| 5 | Anus | Incision | 7 | 7 | Spot on touch | Neuroma; ex-posed fibers | 1 |
| 6 | Finger | Laceration | 12 | 4 | Sharp, spot | Large neuroma | 11 |
| 7 | Scalp | Laceration | 96 | ? | Sharp, spot | Long neuroma | 1 |
| 8 | Nose | Ulcer | 12 | 3 | Intense itching | Small neuroma | 4 |
| 9 | Ear | Puncture | 24 | 24 | Sharp spot and mild diffuse | Neuroma and inflammation | 1 |
| 10 | Neck | Excision of keloid | 3 | 3 | Spot on keloid | Neuroma | 1 |
| 11 | Chest | Laceration keloid | 168 | 12 | Diffuse on keloid | Inflammation | 5 |
| 12 | Abdomen | Hysterec-tomy | 2 | 2 | Spot | Inflammation | 4 |

*Case 3 was an autopsy specimen. Case 11 had recurrence of pain three months after excision of the keloid. All other cases were free of symptoms.

MATERIAL AND METHODS

The present report is a study of twelve cases* of painful scars in various locations. Clinical tests were made of sensation, especially for points of hypersensitiveness to pinprick and to pressure. After excision of the painful area, the points of tenderness were examined histologically in serial section impregnated for nerve fibers by the Gros method.† Routine hematoxylin and eosin sections were made for comparison.

Small blocks of excised scar, properly oriented by drawings, were fixed immediately after operation in neutral 10 per cent formalin. After a period of fixation of at least four weeks, and preferably eight weeks or more, with several changes of formalin in glass-stoppered bottles, rather thick serial frozen sections were cut and placed in individual dishes. Each section was then impregnated separately under microscopic control.

In most instances a follow-up study of the postoperative course was possible and demonstrated relief of symptoms after excision. A preliminary note on the clinical aspects of these cases has been published.¹⁴ In Table I the clinical data are summarized.

*Case 1 was treated at the University of Chicago Clinics, and the excised tissue was studied at the University of Pittsburgh. In three other cases the specimens were presented by others, in two of which I had the opportunity of examining the patient before excision of the scar.

†My thanks are due to Professor Jan Boeke and to Dr. L. K. Akkeringa of the University of Utrecht, Holland, for teaching me the refinements of the silver impregnation methods.

PAINFUL SCARS

F. E. KREDEL, M.D.

CHARLESTON, S. C.

(From the Department of Surgery, Medical College of South Carolina)

FORTUNATELY only a small proportion of cutaneous scars resulting from surgical and accidental wounds remain painful or tender. However, occasional cases are seen in which painful scars are not only annoying to the patient, but may be sufficiently disabling to demand treatment. That excision of the entire scar will usually relieve the symptoms has been well established. Less is known about the cause of the pain, and the fact that only a small area on the scar may be responsible for the symptoms has not been emphasized.

Quain and Eggers,¹ in 1918, demonstrated in seven cases that painful appendectomy scars can be relieved by excision and suggested that inclusion of nerve fibers in the scar may be a cause of pain. Corner² emphasized the importance of persisting infection as a cause of painful scars, especially in amputation stumps, and was able to culture microorganisms about the regeneration neuroma in a wound which had been healed for three years. Corbett³ pointed out that small nerves may be the site of painful neuromas that may be seen grossly. Clinton⁴ found in cases of subcostal neuritis a small neuroma-like swelling of the intercostal nerves as they passed the tips of the last few ribs. Baneroff⁵ reported four cases of painful right rectus incisions in which block anesthesia as a diagnostic procedure caused temporary cessation of pain. Relief followed excision of the scar. Neuromas were suspected although they were not seen in routine pathologic sections. Leriche⁶ and, more recently, Pozzan⁷ have reported favorable results in painful scars after the repeated injection of procaine hydrochloride. Thomas⁸ relieved the pain of an inguinal scar by proximal section of the ilioinguinal nerve. Molotkoff⁹ ventured the opinion that, in painful amputation stumps, abnormalities in the terminal ramification of the pain fibers were of more importance than neuromas of large nerve trunks. He advised high section of all the sensory nerve supply to the affected region and performed this procedure in eleven cases.

A few histologic studies have been reported by anatomists on nerve regeneration in cutaneous scars. Jäger and Traum¹⁰ found that superficial regenerating fibers did not acquire encapsulated corpuscles but terminated in free endings. Tsunoda, Hamada, and Arimoto¹¹ noted that nerve fibers growing into scarred and inflamed areas acquire their protecting sheaths only at a late stage, if at all, as Corner² had previously mentioned. Klein¹² reported that minute amputation neuromas

Presented at the meeting of the Society of University Surgeons at New York, N. Y., February 9 and 10, 1940.

come quite destitute of sheath cells as they approach the ulcerated surface. Several encapsulated end organs of the Golgi-Mazzoni type are also supplied by fibers from the region of the neuroma. There is some diffuse inflammatory infiltration, but it is not in close relation to the neuroma or its branches.

A painful spot on a stellate scar of the finger tip in Case 6 showed a dense globular neuroma about 0.6 or 0.8 mm. in diameter, embedded in dense collagenic fibrous tissue (Fig. 3). This was the case of Dr. H. Bowen.

In Case 7 a linear scar in the occiput contained an exquisitely tender spot. The specimen from Dr. J. P. Evans of Cincinnati showed an elongated dense neuroma just superficial to the galea and originating from a fairly large branch of an occipital nerve. This neuroma with its ramifications covers an area 10 by 3 mm.



Fig. 2.—Case 5. Neuroma in scar at anus, with nerve fibers exposed on ulcerated surface.

A scar on nose after x-ray treatment of ulcer in Case 8 contained a loose plexiform neuroma in its deep portions. The specimen was sent by Dr. J. A. Sasser of Conway, S. C.

In Case 9 there was a keloid of the ear which showed slight general tenderness and a single painful spot. There were numerous small foci of round and plasma cells, some of which, particularly at the margins, were adjacent to or surrounded small nerve fibers. The sensitive spot contained a small loose neuroma embedded in fibrous scar.

SUMMARY OF MICROSCOPIC FINDINGS

In Case 1 the segment, 6 by 2 mm., excised from a sear on the foot showed a small plexiform neuroma composed largely of single nerve fibers poorly supplied with protecting sheaths midway in the scarred corium and in close relation to a venule.

In Case 2 there was excision of two painful areas on a mastectomy sear. Fig. 1 shows a large regeneration neuroma deep in the sear just superficial to the subcutaneous fat. The size of the involved nerve bundles suggests their origin from a relatively large nerve trunk. Branches of this neuroma extend for considerable distances into the sear and are turned back before reaching the surface. They tend to be directed parallel to the densely packed collagenic fibers.

In Case 3, was a painful spot on a mastectomy sear, containing an excessive plexiform neuroma, from which radiated numerous long and undulating fibers compressed in dense sear tissue.

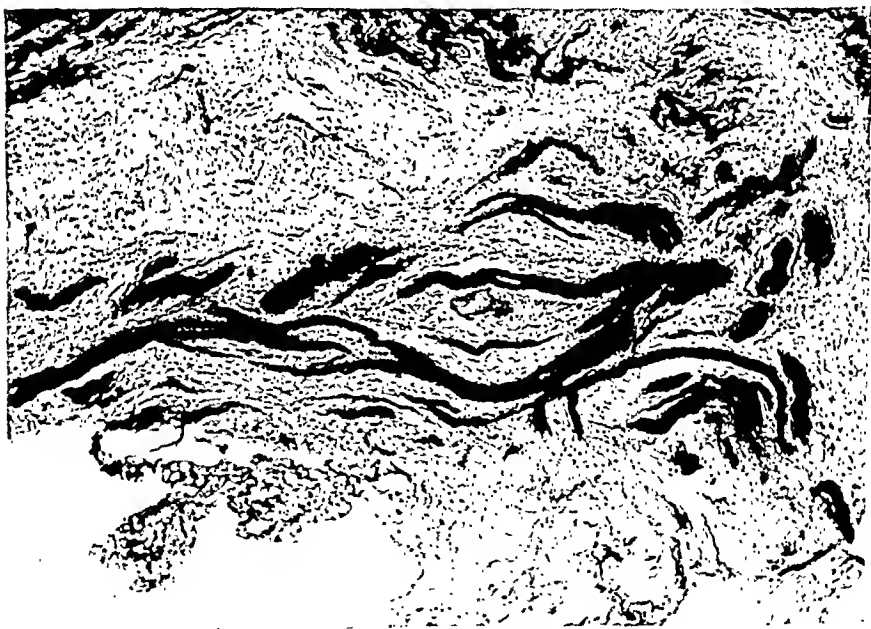


Fig. 1.—Case 2. Neuroma with rather large nerve bundles in mastectomy sear overlying subcutaneous fat.

On a mastectomy sear in Case 4 were two spots which contained several small neuromas immediately beneath the corium.

In Case 5 there was a minute nodule 2 by 2 mm. at the anal orifice which was exquisitely tender to touch as well as pressure. Sections showed deep in the nodule a neuroma of large nerve bundles. Fibers from the neuroma can be traced to the surface, a small area of which is eroded (Fig. 2). As can be seen, these small fibers apparently be-

In Case 10 there was a massive keloid of the neck with a sensitive spot on the scar after partial excision. Excessive plexiform nerve regeneration with some inflammatory infiltration was present at the painful spot.

In Case 11 was a diffusely tender keloid over the sternum, with recurrence of discomfort three months after excision. Sections showed numerous regenerated nerve fibers coursing for great distances through the scar parallel to the surface. These fibers had fairly adequate sheaths and were single or in small bundles of from two to four fibers. Numerous areas of cellular infiltration, in some instances minute abscesses, surrounded the nerve fibers (Fig. 4). Neuromas were not seen.

In Case 12 there was a painful spot on a recently healed laparotomy scar, with many areas of inflammation about neurovascular bundles and regenerating nerve fibers. No neuromas were present.

DISCUSSION

The histologic findings in these cases indicate that pathologic forms of nerve regeneration in relation to cicatricial tissue are of importance in the production of painful scars. In ten of the twelve cases, a neuroma demonstrated microscopically at the point of maximum hyperalgesia seemed the chief cause of pain and tenderness. In two cases, inflammatory changes seemed responsible for the pain. One of these was a diffusely tender keloid, and the other, a recently healed laparotomy wound. It seems reasonable to assume, therefore, that a localized point of tenderness in an old scar in all probability indicates a neuroma.

The neuromas have been situated, for the most part, rather deep to the surface near the region where ingrowing cutaneous nerve fibers first encounter dense or infected scar tissue. Excision of a painful spot should, therefore, include the full thickness of the scar. Only that small portion of a painful scar containing a tender area need be removed to effect a cure. This fact becomes of importance when excision of the entire scar is undesirable and a lesser procedure on an ambulatory patient will suffice. Cases in point are long mastectomy or laparotomy scars, as well as multilinear stellate scars, where complete removal might entail complicated plastic maneuvers or unnecessary sacrifice of tissue. In recent cases of a few months' duration where the degree of pain does not make relief imperative, a period of observation may be indicated. Kredel and Evans¹⁵ have reported in pedicle skin flaps that hyperalgesic points appearing at the borders of a scar may gradually disappear in the course of several months. The disappearance of pain in recent scars may be explained by the subsidence of inflammation or by the fact that the irritable regenerating nerve fibers atrophy or acquire their protecting sheaths of myelin and Schwann cells.

As regards the recognition pathologically of cutaneous neuromas, routine methods of examination are of little aid. Grossly, although reaching the size of several millimeters, the neuromas are difficult to distinguish from the scar in which they are embedded. Sections, unless cut exactly at the sensitive spot, may miss the neuroma altogether. Even

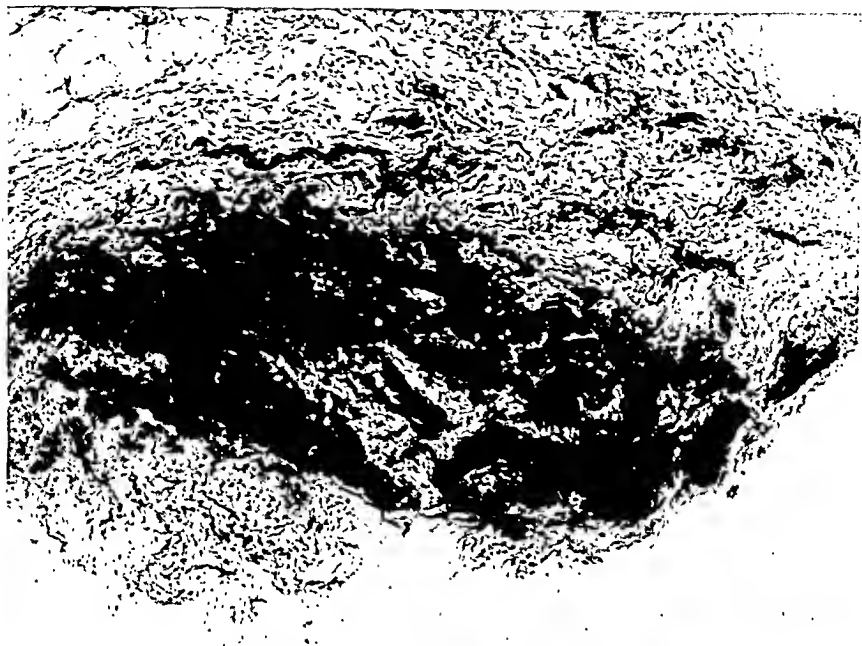


Fig. 3.—Case 6. Dense neuroma at base of scar on finger tip.

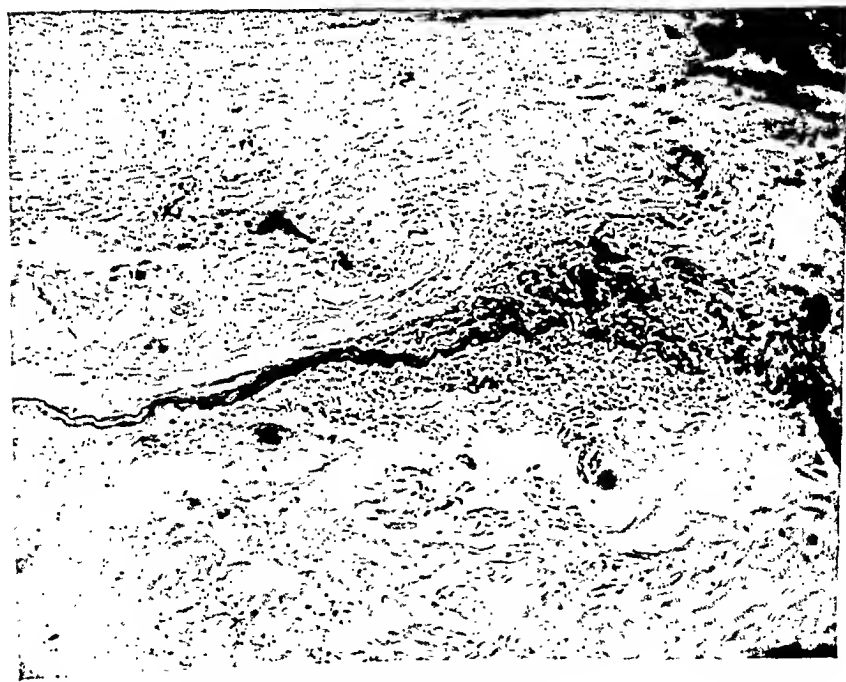


Fig. 4.—Case 11. Focus of chronic inflammation involving regenerating nerve fibers in keloid over sternum.

EXPERIMENTAL STUDIES IN TRANSPLANTATION OF THE ADRENAL GLAND

J. ENGLEBERT DUNPHY, M.D., AND JOHN L. KEELEY, M.D., BOSTON, MASS.

(From the Laboratory for Surgical Research, Harvard Medical School)

MANY attempts to transplant the adrenal gland in the dog have proved unsuccessful.¹⁻³ Failures have been attributed, in part, to the irritating properties of the degenerating medulla which produces massive necrosis in the tissues to which the transplant is made.⁴ This has led some investigators to remove the medulla prior to transplanting the cortex of the gland, and it is now rather generally accepted that in small animals adrenal transplants undergo a necrosis which is followed by a regeneration from the capsule of the cortex only.⁵⁻⁷ In the dog Levy and Blalock⁸ succeeded in transplanting the kidney together with the adrenal to the neck, re-establishing the blood supply by suture of vessels. Subsequently the kidney was removed and viable transplants of both cortex and medulla of the adrenal remained. In a previous communication⁹ successful transplantation in the dog of the adrenal to the ovary was described. This was accomplished by grafting without suture of blood vessels, and in such preparations viable transplants of both cortex and medulla were obtained. What appears at present to be the most satisfactory method of accomplishing such a transplantation is herein described and evidence of the functional activity of both the cortical and medullary portions of the graft is presented.

The experimental procedure is as follows: Healthy mongrel bitches are used. In the early experiments it was thought that small animals (5 to 10 kg.) were more suitable, but with more experience with the technique successful transplantations can be obtained in larger ones (15 to 20 kg.). Operations are performed aseptically under sodium pentobarbital (nembutal, Abhott) anesthesia. The procedure is divided into three operative stages. At the first stage the left adrenal gland is exposed through an oblique subcostal incision (Fig. 1 insert). The lower pole of the gland is freed by blunt and sharp dissection without dividing the lumboadrenal vein. The ovary and salpinx on that side are then mobilized and drawn up over the anterior surface of the renal pedicle to the bed of the adrenal (Fig. 2). In some of the early experiments a small fragment of each gland was then excised and the raw surfaces united with sutures (Fig. 2 *a*). It is more satisfactory to incise the free edges of the glands, partially bisecting them and then interlocking or "sandwiching" the two together (Fig. 2 *b*). This position is then maintained by mattress sutures of fine silk. The wound is closed and at a second operation, which is performed three or more weeks later, the

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when through the proper area, thin sections stained by ordinary methods show little. Thicker sections may supply a clue if the sheaths of larger nerve bundles can be seen. But a neuroma whose fibers are deficient in sheath of Schwann cells can be demonstrated satisfactorily only by special methods for nerve fibers.

CONCLUSIONS

1. Painful and tender scars should be examined for local points of hypersensitiveness.
2. Simple excision of these sensitive spots will relieve the symptoms without removal of the entire scar.
3. Neuroma formation of tiny cutaneous nerves is the most important factor in the production of painful cutaneous scars of long duration.
4. Inflammatory changes may be the cause of pain in recently healed scars.
5. Prolonged healing with subsequent excessive scar tissue about regenerating nerves is apparently conducive to the production of painful neuromas.
6. Demonstration of minute cutaneous neuromas may require the use of special histologic methods for the impregnation of nerve fibers.

SUMMARY

The clinical and histologic findings are presented in twelve cases of painful cutaneous scars. In ten cases, microscopic neuromas were found at the points of tenderness. Relief of symptoms followed excision of the painful areas alone.

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adrenal is separated from its normal neurovascular supply and transplanted together with the ovary (Fig. 3) to the lower abdomen where it is sutured to the peritoneum of the anterior abdominal wall. The final stage, removal of the right adrenal, is performed about one month later. The right adrenal can be transplanted by the same technique, but more difficulty is encountered in freeing the right gland because of its proximity to the vena cava. For this reason usually the left adrenal is transplanted and the right adrenal excised.

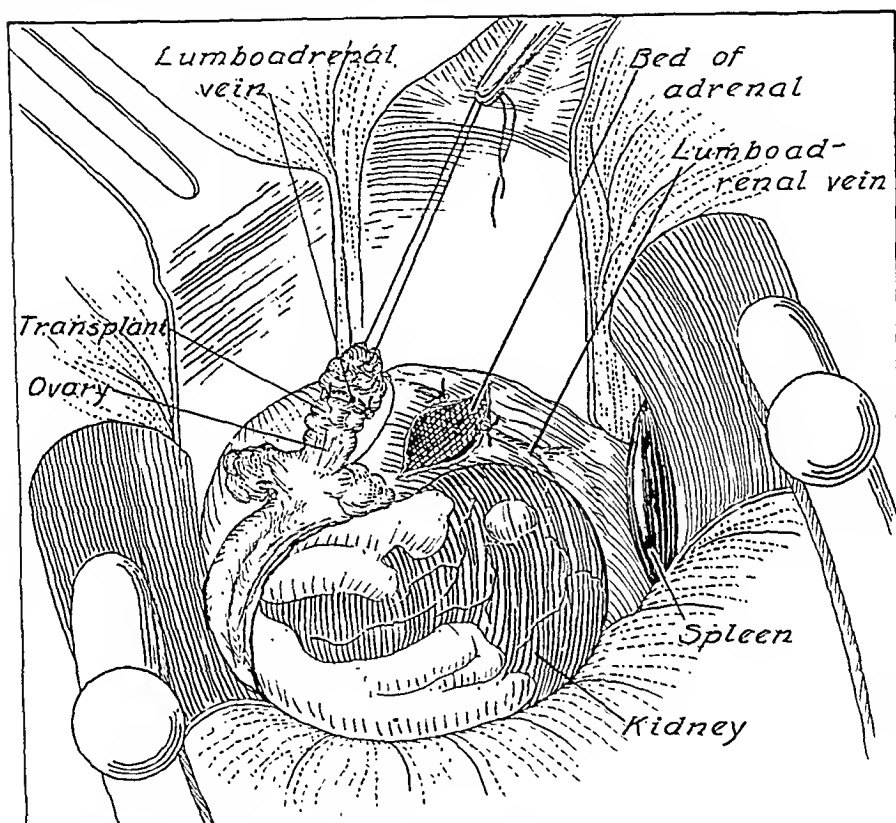


Fig. 3.—This, the second stage of the operation, is performed one month later, at which time the lumboadrenal vein is divided and the adrenal is separated from its normal neurovascular connection. The gland is then transplanted together with the ovary into the peritoneal cavity.

It is interesting that by this method there is no acute physiologic deficiency of adrenal tissue at the time the transplant is made, as the opposite adrenal is intact. Similar exceptions to Halsted's¹⁰ "law of deficiency" have been noted by Levy and Blalock⁸ and by Shambaugh.¹¹

To date eight successful transplantations have been made. The animals appear to live indefinitely after transplantation of the left and excision of the right adrenal. One is alive and in good condition after twenty-three months. In four experiments the transplant was excised under aseptic conditions and the animals were allowed to recover from the anesthesia. Death from adrenal insufficiency occurred in two, five,

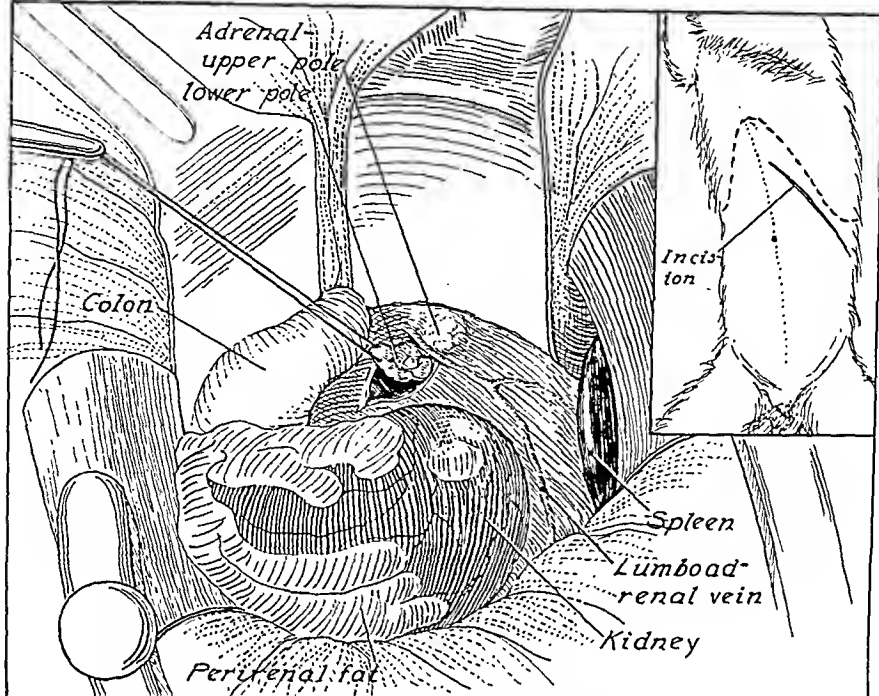


Fig. 1.—The lower pole of the left adrenal gland is exposed. Note that the lumbo-adrenal vein is not disturbed.

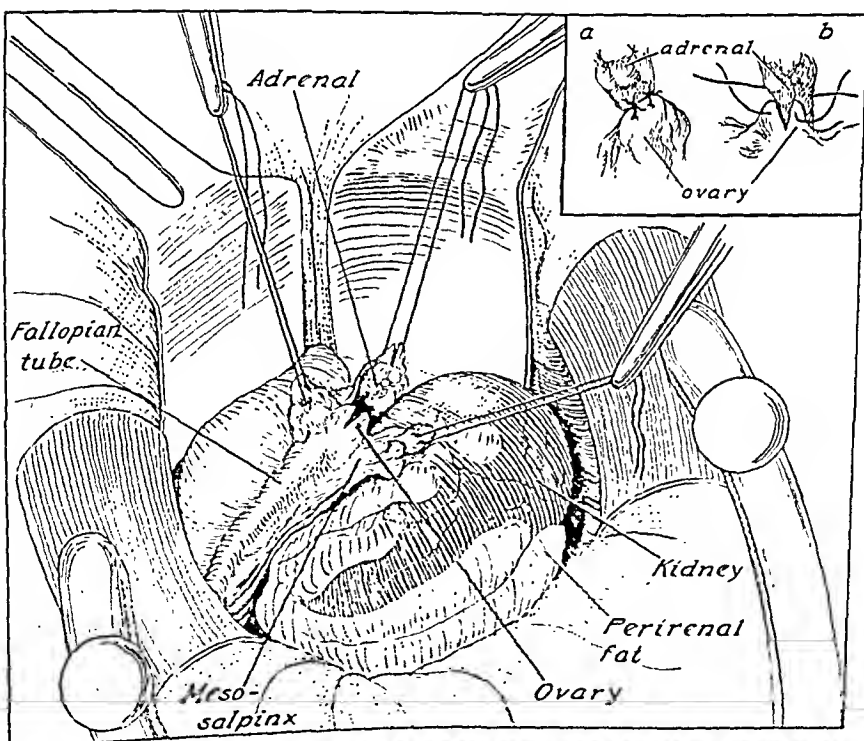


Fig. 2.—The ovarian pedicle is mobilized and the ovary and adrenal are about to be united by interlocking the partially bisected free edges of the glands.

smaller than normal, but the sharp demarcation between cortex and medulla is recognizable. On microscopic examination (hematoxylin and eosin and eosin-methylene blue) no significant variations from the normal are found in the cortical or medullary cells. The contour of a transplant removed six months after transplantation is shown in Fig. 4. In-



Fig. 5.—Photomicrograph showing the area between the adrenal and the ovary in a six-month transplant. Except for the presence of the silk suture, the two glands appear almost as a single organ. ($\times 25$, hematoxylin-eosin stain.)

cluded in the section are portions of the Fallopian tube, ovary, and adrenal. Note that the normal contour of the adrenal, including the medulla, is well preserved. Between the two glands is a thin layer of vascular connective tissue. How little the appearance of the two glands is altered by the transplantation is shown in Fig. 5, in which, except for the silk suture, ovary and adrenal appear as one organ. At a higher

seven, and nine days respectively. Following excision of the transplant anorexia was the first symptom to appear. Gradually the animals became weak and apathetic, refusing all food and water. There was a terminal fall in the serum chloride and blood pressure in the two animals in which these determinations were made. The findings at autopsy were



Fig. 4.—Photomicrograph showing the contour of a transplant six months after transplantation. Fallopian tube, ovary, and adrenal are included in the section ($\times 13$, hematoxylin-eosin stain).

those usually associated with adrenal insufficiency. There was marked congestion in the viscera, particularly in the lungs, pancreas, and upper gastrointestinal tract, and to a lesser extent in the kidneys and liver. In no instance was accessory adrenal tissue found, although microscopic studies were made of tissue from the usual location of the glands.

The characteristic appearance of the adrenal gland is well preserved in the transplanted tissue. The medullary portion of the graft is always

supply to the central portion of the gland. By the method described above, a new blood supply has been partially established before the gland is deprived of its normal supply. The reason for the reduction in size of the medulla may be a certain deficiency of vascular supply, but this does not appear to alter the histologic appearance of the surviving cells (Fig. 8).

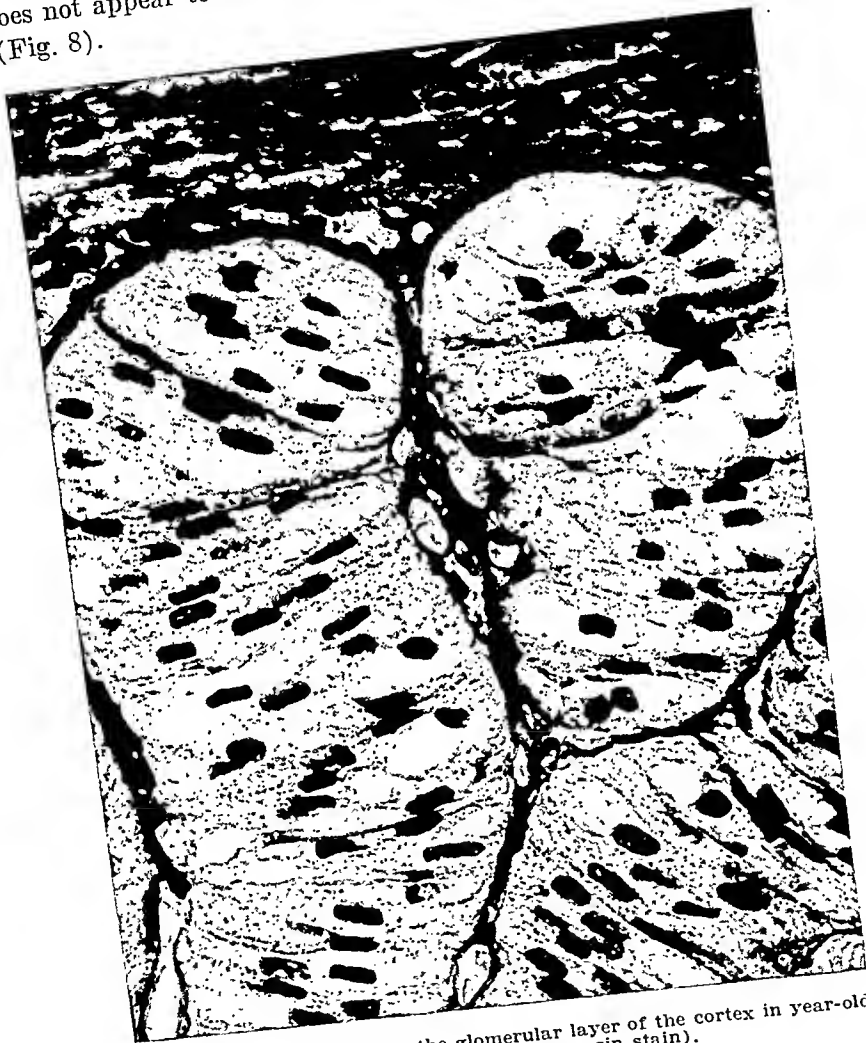


Fig. 7.—Photomicrograph showing the glomerular layer of the cortex in year-old transplant ($\times 300$, hematoxylin-eosin stain).

Ganglion cells are easily demonstrated in the capsule of the gland and unmyelinated nerve fibers are found in both the capsule and medulla. No myelinated nerve fibers are found. This is similar to the observation of Elliott¹³ and Hollinshead,¹⁴ who found that, although myelinated nerve fibers degenerate after division of the sympathetic nerve supply to the adrenal, there is a persistence of unmyelinated fibers. Such nerves probably arise from intrinsic ganglion cells. Levy and Blalock⁵ also found only unmyelinated nerve fibers in transplanted adrenals.

power (Fig. 6) the cortical zones and medulla are more readily discernible. There is no hypertrophy or hyperplasia of the gland. The zona glomerulosa (Fig. 7) is well preserved without evidence of degenerative changes. There is less vacuolization of the cells in the fasciculata than usual, but here again no definite histologic evidence of malfunction is noted by the ordinary staining methods.



Fig. 6.—Photomicrograph showing the various layers of the cortex and the medulla in year-old transplant ($\times 76$, hematoxylin-eosin stain).

The excellent preservation of the medullary cells in these transplants (Figs. 6 and 8) indicates that, as Turner and his co-workers¹² have suggested, the principal reason for the failure of medullary transplants has been the difficulty in establishing, sufficiently soon, an adequate blood

vein has been so bright red as to be indistinguishable from arterial blood, and on determining the oxygen content of the arterial and venous blood one often finds an unusually low arteriovenous difference. This, however, is not a constant finding, for, after exercise or while under anesthesia, there may be a high arteriovenous difference. The total blood and plasma volume has been determined in two animals before and after transplantation of the adrenal. In both there was a slight decrease in volume.*

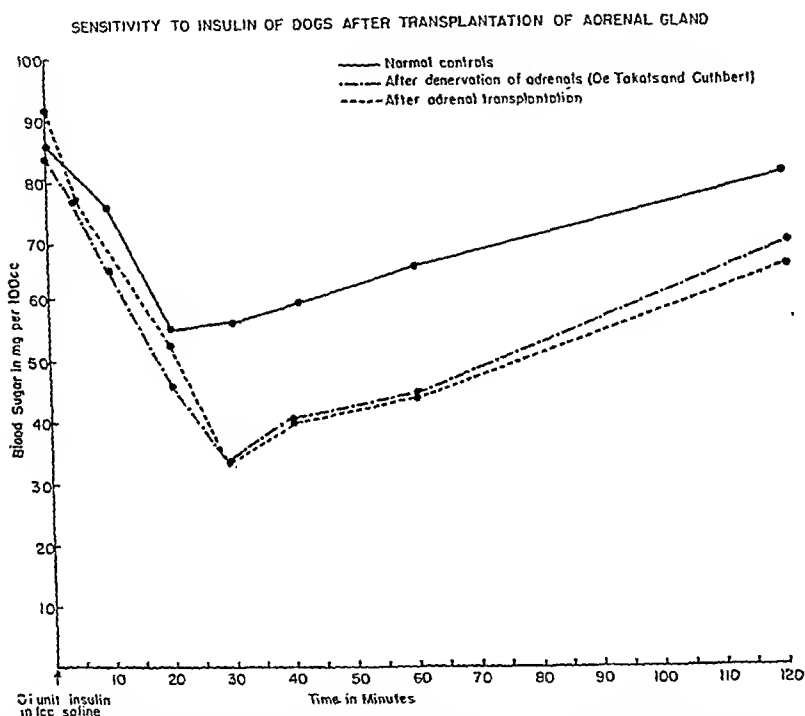


Fig. 9.—Curves showing the sensitivity to insulin of dogs as indicated by the fall in the blood sugar following the intravenous injection of 0.1 unit of insulin in 1 c.c. of normal saline solution.

As previously stated, the functional activity of the cortical portion of the transplants has been demonstrated in four experiments by the death of the animals following excision of the graft. No accessory adrenal tissue was found at autopsy and, if present, it obviously was not sufficient to maintain the life of the animal after removal of the transplant. Although the cells of the medulla appear viable, the function of this portion of the gland is considerably altered. It is well known that the secretion of adrenalin in response to various stimuli produces a transient hyperglycemia. Using this test as an indication of adrenalin secretion, Levy and Blalock could find no evidence of function of the medullary portion of transplanted adrenal glands. Even after the intravenous injection of acetylcholine, which is thought by Feldberg and

*The determinations were made by John G. Gibson, 2nd, by the method described by Gibson and Evans.¹²

The behavior of the animals following autotransplantation of the adrenal gland is not altered. Their general appearance is the same. They are as active as normal, eat well, and either gain or maintain their weights. None of these animals have contracted distemper, although several have been exposed to the disease at varying periods during their course in the laboratory. In two experiments the blood pressure was determined by the arterial puncture method before and at varying intervals for a year after transplantation. No significant variations were noted. The normal fasting levels of sugar, nonprotein nitrogen, albumin, globulin, calcium, and phosphorus in the blood have not been altered by transplantation of the adrenal gland in the two experiments in which these determinations were made.

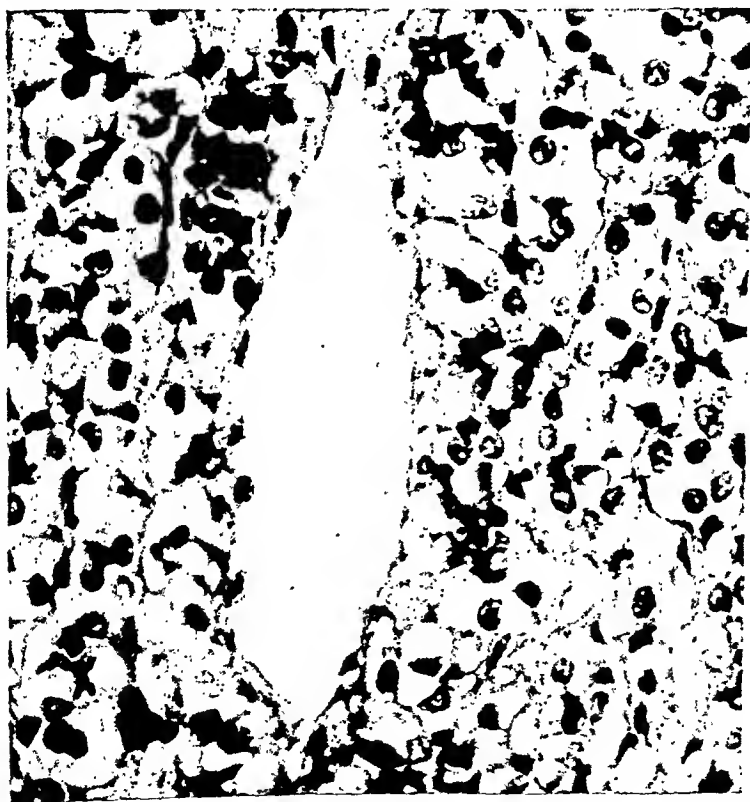


Fig. 8.—Photomicrograph showing the medulla of year-old transplant ($\times 260$, hematoxylin-eosin stain).

Although the general appearance and behavior of the animals is not altered and they seem able to withstand the ordinary hazards of laboratory existence, certain variations from the normal have been noted. These animals are extremely sensitive to sodium pentobarbital so that one-half the usual dose is sufficient to produce a full surgical anesthesia. Also, on a number of occasions the blood withdrawn from the jugular

vein has been so bright red as to be indistinguishable from arterial blood, and on determining the oxygen content of the arterial and venous blood one often finds an unusually low arteriovenous difference. This, however, is not a constant finding, for, after exercise or while under anesthesia, there may be a high arteriovenous difference. The total blood and plasma volume has been determined in two animals before and after transplantation of the adrenal. In both there was a slight decrease in volume.*

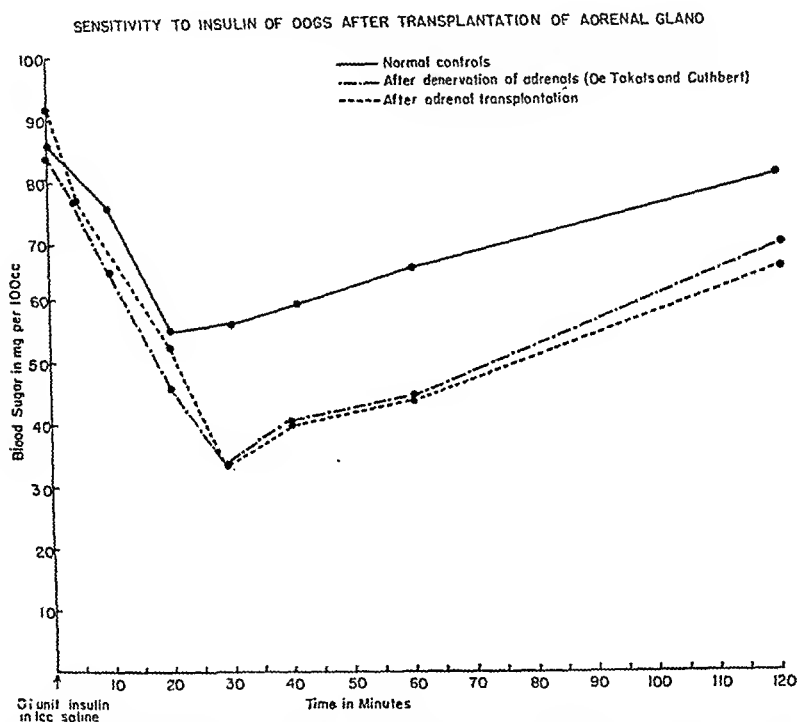


Fig. 9.—Curves showing the sensitivity to insulin of dogs as indicated by the fall in the blood sugar following the intravenous injection of 0.1 unit of insulin in 1 c.c. of normal saline solution.

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his associates¹⁶ to be the humoral transmitter of sympathetic impulses to the adrenal medulla, no hyperglycemic response was observed. Similar observations were made in the present study. The sugar tolerance of a dog following transplantation of the adrenal is similar to that seen after denervation of the adrenals.¹⁷ Thus, there is a markedly increased sensitivity to insulin. The blood sugar curves following the injection of 0.1 unit of insulin intravenously in normal dogs, in those with transplanted adrenals, and in those with denervated adrenals is shown in Fig. 9. Note how closely the curves of the denervated and transplanted glands approximate each other. Although these various observations indicate that adrenalin is not secreted into the blood stream, they do not prove that the medullary cells are incapable of producing adrenalin.

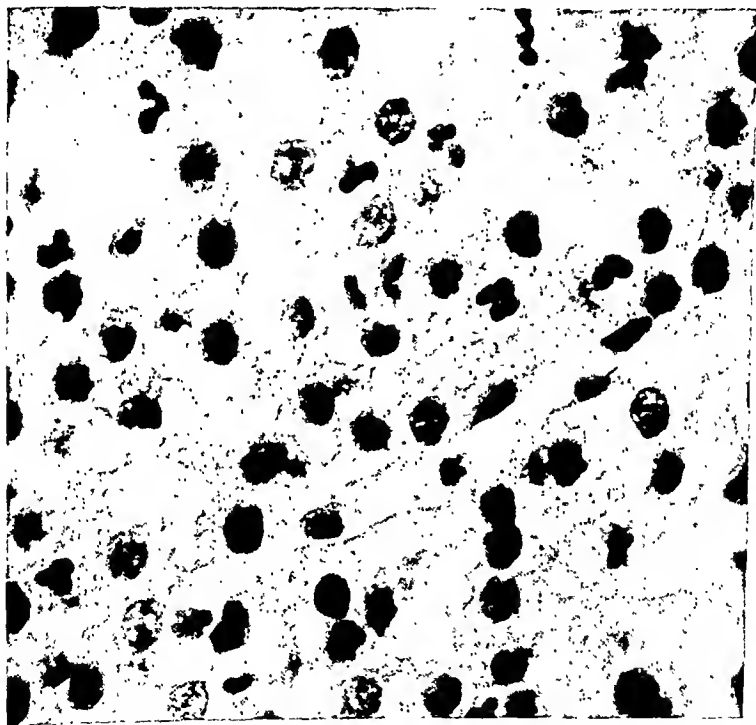
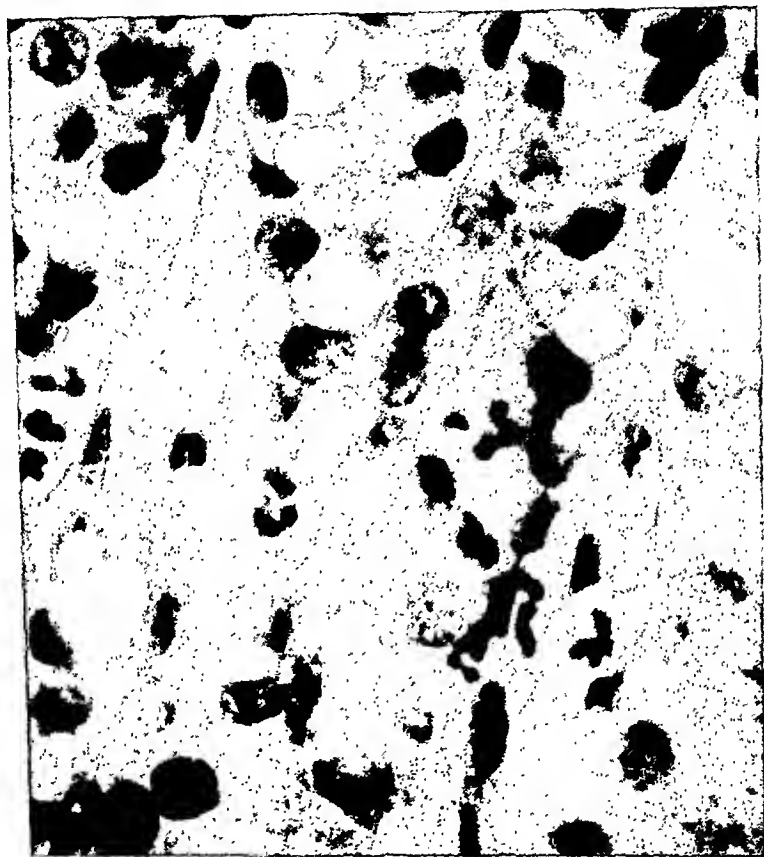


Fig. 10.—Photomicrograph showing the cells of the zona fasciculata of an intact adrenal gland ten hours after thermal trauma. There is swelling of the cortical cells and invasion of the area by polymorphonuclear leucocytes. ($\times 1130$, hematoxylin-eosin stain.)

Despite the fact that the intravenous injection of acetylcholine in these experiments, as well as in Levy and Blalock's, failed to produce a hyperglycemic response, it seemed possible that adrenalin might be present in the gland and that the formation of acetylcholine at nerve endings within the medulla was necessary for active secretion into the blood stream. Accordingly, in two experiments the grafts were excised twelve and fourteen months after transplantation and assayed for adrenalin and acetylcholine. The assays were made by K. Lissak of the

Department of Physiology by a method which he has described.¹⁸ By this method the normal adrenal of the dog gives a positive test for both adrenalin and acetylcholine-like substances. In the transplanted adrenal definite evidence of an adrenalin-like substance, in amounts of 80 γ (gamma) per gram, was found, but there was no evidence of acetylcholine. These observations a year or longer after transplantation indicate that the medullary cells not only appear viable histologically but are apparently capable of producing an adrenalin-like substance. The



A.

Fig. 11 A and B.—Photomicrographs showing the cells of the zona fasciculata in a six-month-old transplanted adrenal eight hours after thermal trauma. The same histologic changes noted in the intact adrenal are found in the transplanted adrenal. ($\times 1130$, hematoxylin-eosin stain.)

absence of acetylcholine together with the inability of the animal to mobilize adrenalin into the blood stream, although it is present in the gland, lends confirmation to the hypothesis maintained by Feldberg that acetylcholine is the humoral transmitter of sympathetic impulses to the adrenal medulla and that its formation at nerve endings within the medulla is essential for the release of adrenalin into the blood stream.

Although the exact role of the adrenal in various forms of shock is not clearly understood, it is known that following severe thermal trauma

pathologic changes in the gland are a constant finding at post mortem.^{10, 20} Further evidence of the function of the transplanted adrenal is the fact that it shows the same histologic changes after thermal trauma as the normal gland. These consist of swelling of the cortical cells, particularly in the zona fasciculata and to a lesser extent in the zona reticularis, and an invasion of the area by polymorphonuclear leucocytes. The glomerular zone is not involved. These changes, as seen in a normal intact adrenal several hours after severe thermal trauma, are shown in Fig. 10. It is interesting that the transplanted adrenal, separated from its normal neurovascular connections and thus free from a bombardment by sympathetic stimuli, should show a similar alteration



Fig. 11B.—See page 115 for legend.

of the cortical cells and infiltration with polymorphonuclear leucocytes (Fig. 11 A and B). This transplant was removed eight hours after the onset of shock from severe thermal trauma. The transplantation had been completed sixteen months previously and the animal had remained in excellent health until the time of the acute experiment. It is evident that the pathologic changes which occur in the adrenal after thermal trauma are not of neurogenic origin.

SUMMARY

The technique of autotransplantation of the adrenal gland of the dog by grafting it to the ovary is described in detail. Such transplants are composed of viable cells of both cortex and medulla and are sufficient

to maintain the life of the animal for indefinite periods of time. Successful autotransplantation of the adrenal by this method can be accomplished without a marked physiologic need for the graft at the time of transplantation.

The functional activity of the cortical portion of the grafts has been proved in four experiments after a period of four to fourteen months by the death of the animal from adrenal insufficiency following removal of the grafts. Although there is no evidence that adrenalin is secreted into the blood stream after transplantation of the adrenal, biologic assays of the grafts have demonstrated the presence of an adrenalin-like substance. There is no acetylcholine in the transplanted adrenal. Following the shock of severe thermal trauma, the same histologic changes are found in the transplanted adrenal as are noted in the normal intact adrenal.

The authors wish to thank Dr. Orville T. Bailey of the Department of Pathology for the photomicrographs and Dr. K. Lissak, formerly of the Department of Physiology, for the biologic assays of the transplants.

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Editorials

The Society of University Surgeons and the Need for a Surgical Forum

THE major portion of this issue of SURGERY is devoted to publication of papers of the second annual meeting of the Society of University Surgeons. This organization, the membership of which is composed of young men who have obtained their training in university surgical clinics, had its origin less than a year ago. The founders' group was comprised of surgeons from the following ten university medical schools: Chicago, Cincinnati, Columbia, Cornell, Harvard, Johns Hopkins, Rochester, Vanderbilt, Washington (St. Louis), and Yale. Fifty men were admitted to active membership at the first annual meeting held at Rochester, N. Y., in February, 1939. Upon arriving at the age of 45 years, men will retire automatically from active membership and become senior members. The qualifications for membership are defined as follows:¹

1. The completion of at least one year as surgical resident in a university medical college hospital, maintaining a recognized resident system of postgraduate instruction.

2. Appointment to an official position on a surgical service of a university hospital.

3. Recommendation for membership by a member of the Society connected with the institution with which the applicant is associated.

4. A practice limited to surgery or the surgical specialties.

The aims of the Society of University Surgeons are the advancement of the art and science of surgery by:

1. The encouragement of its members to pursue original investigations both in the clinic and in the laboratory.

2. The development of methods of graduate teaching of surgery with particular reference to the resident system.

3. Free and informal interchange of ideas pertaining to the above subjects as a limited membership and common aims make possible.

One of the most urgent and obvious needs among surgical organizations in this country has been a surgical forum to which young men can bring their contributions and secure an audience. It is to be hoped that this newly formed Society of University Surgeons will satisfy, in part, this want. It is to be regretted that existing surgical societies have been slow to include a generous number of representative progressive young surgeons in their membership. For out of that group come the surgical leaders of tomorrow. The late William J. Mayo felt keenly

that the wisdom of age and experience should be exchanged freely with the enthusiasm of youth and that both old and young would benefit by the barter. The most original contributions to surgery, in the main, have their origins in the minds of young men. Exclusion of such men from membership in established surgical societies appears inconsistent with the expressed primary objective of all surgical societies; namely, the advancement of the art and science of surgery.

True enough, if a young surgeon has something worth while to say, surgical journals and other medical publications provide him with an avenue for making his ideas known. The particular merit of special societies is that their meetings furnish the individual the opportunity for crystallizing his ideas through discussion. It affords him also the opportunity of seeing and hearing and learning to know some of his colleagues. The interests of the membership, as a whole, of societies are served best by provision for the most original and stimulating papers within the scope of concern of its auditors, whether from the membership or by invitation, that the occasion can provide. It is to be admitted freely that the number of papers evincing real evidence of creative thought or distinctive achievement available for reading at the meetings of most societies is not numerous. Original thinking is the most difficult kind of labor and most of us spare ourselves its pains or are incapable of sustained thought in unchartered channels. In extenuation of this circumstance, it must be said that the yoke of duty and responsibility for the daily tasks hangs heavily on the surgeon. Much of his time is occupied in striving to perfect himself in those compartments of skill and knowledge which contribute to his effectiveness and the welfare of his patients.

The functions of a university are to teach and to think. Like a university, much of the activity of a society of like-minded individuals (including surgeons) is taken up by the interpretation or re-echoing of the recorded accomplishments of others. To this group of men, into which category most of us come, who essay to present papers before surgical gatherings, Glenn Frank has given the designation of "salesmen of knowledge." Moreover, the art and the science of surgery are in far greater need of the creative rather than of the interpretative mind. There appears to be a veritable plenitude of purveyors and caterers of surgical knowledge. In this connection the admonition of Cardinal Newman is not to be forgotten: "He who spends his day in dispensing his existing knowledge to all comers is unlikely to have either leisure or energy to acquire new."

It is interesting to contemplate the fortunes of Murphy and Halsted in their day. Resplendent, as one of the greatest surgical teachers of his time, Murphy's career reached its zenith within his lifetime and his star is growing dim already on the surgical horizon. The influence of Halsted is the lengthening shadow of a great man who made im-

portant contributions to his province of knowledge, but whose contemporary audience of appreciative admirers was not large. Halsted's star is rising and promises to remain luminous in the surgical firmament for a long time to come.

Much serious thought has been devoted recently by American leaders in surgery to the composition, objectives, and the potential influence of surgical societies. In a brilliant address entitled "Samuel Gross Looks in on the American Surgical Association," conducted in the manner of a Socratic dialogue, written in the Erewholmian vein of Samuel Butler, Graham² raised a number of questions concerning the nature of the organization and objectives of the American Surgical Association which are known to every group which has undertaken the responsibility of formulating a society which proposes to radiate a useful influence. In a very informative paper Phenister³ has traced the origins and outlined the objectives and recounted the influences of the national surgical societies of a number of countries.

In his interesting monograph "The First Twenty-Five Years of the German Surgical Society" Trendelenburg relates how matters of composition as well as size of membership, audience, and nature of program were discussed by Laugenbeek, Volkman, Baner, Simon, and Billroth in the formation of the German Surgical Society. Professor Billroth inclined to the development of a free informal group in which chatty types of papers could be presented with a free admixture of intimate social intercourse. Laugenbeek, on the contrary, insisted on a more formal type of organization which would radiate the influence of German surgery widely. The years have shown the wisdom of Laugenbeek's judgment.

The purpose of the Society of University Surgeons, it is to be hoped, will concern itself more with the advancement of knowledge than with its diffusion. If this or any other constituted surgical group satisfies the pressing need for a surgical forum before which the most creative thought and original achievement in American surgery can secure an audience, it will fill a long-felt want, exert a large and important influence, and contribute richly to surgery.

Nowhere in the world have surgeons interested themselves so much in the experimental approach to surgery as here. Yet, no regular agency exists which makes it possible for young men interested in and pursuing the lifelong study of surgery to bring their researches before established surgical bodies. They can, it is true, often obtain an audience before a branch of the American Federated Societies comprising the American Physiological Society, the American Society of Biological Chemists, the American Society for Pharmacology and Experimental Therapeutics, and the American Society for Experimental Pathology. But, why should not these men have the opportunity of an audience from surgeons and why should surgeons be denied the privilege of hearing young men,

in their formative years, recite their own achievements? Must a young man receive recognition for his accomplishment before another audience before surgeons will deign to hear him? Surgical societies, whose primary purpose has been the dissemination of surgical knowledge, will do well to lend serious consideration to the matter of the establishment of a *surgical forum* before which the best that is new in surgery each year may be presented. Surgery has been advanced more by its science than its art. Why not admit young men whose training and original contributions to surgery indicate that they are made of sterling stuff freely to the privilege of surgical societies? We who are caterers and purveyors of surgical knowledge are too often guilty of "multiplying words without knowledge." Exclusiveness of membership in scientific gatherings and sterility of ideas are frequent companions.

The past never returns, but the character of the future can be determined, in part, by what is done in the present.

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—Owen H. Wangensteen.

Spinal Anesthesia: A Controversial Subject

SPINAL anesthesia has now been before the medical profession for a good many years. To be sure, for a number of these years it was in a poorly developed state as to drugs, indications, and technique of administration. This by gradual progress has now been largely overcome. While less so than in the past, there still exists almost a controversy, at least a striking difference of opinion, as to the value of spinal anesthesia, particularly in abdominal operations and especially in upper abdominal operations. There are those such as we in our clinic who employ spinal anesthesia in practically all abdominal operations, high and low. There are those who would not consider the employment of spinal anesthesia in abdominal operations; and there are all gradations between the two positions.

It is interesting that such a difference of opinion can continue to prevail and it has frequently interested me to try to analyze the situation in terms of why this difference exists. I have been led to do this because, as the head of a clinic, I have a moral responsibility for methods employed in it and because satisfaction with it, almost amounting to enthusiasm for it, forces me to try to ascertain why others do not have the approving interest in it that we in our clinic have.

portant contributions to his province of knowledge, but whose contemporary audience of appreciative admirers was not large. Halsted's star is rising and promises to remain luminous in the surgical firmament for a long time to come.

Much serious thought has been devoted recently by American leaders in surgery to the composition, objectives, and the potential influence of surgical societies. In a brilliant address entitled "Samuel Gross Looks in on the American Surgical Association," conducted in the manner of a Socratic dialogue, written in the Erewhonian vein of Samuel Butler, Graham² raised a number of questions concerning the nature of the organization and objectives of the American Surgical Association which are known to every group which has undertaken the responsibility of formulating a society which proposes to radiate a useful influence. In a very informative paper Phemister³ has traced the origins and outlined the objectives and recounted the influences of the national surgical societies of a number of countries.

In his interesting monograph "The First Twenty-Five Years of the German Surgical Society" Trendelenburg relates how matters of composition as well as size of membership, audience, and nature of program were discussed by Langenbeck, Volkman, Bauer, Simon, and Billroth in the formation of the German Surgical Society. Professor Billroth inclined to the development of a free informal group in which chatty types of papers could be presented with a free admixture of intimate social intercourse. Langenbeck, on the contrary, insisted on a more formal type of organization which would radiate the influence of German surgery widely. The years have shown the wisdom of Langenbeck's judgment.

The purpose of the Society of University Surgeons, it is to be hoped, will concern itself more with the advancement of knowledge than with its diffusion. If this or any other constituted surgical group satisfies the pressing need for a surgical forum before which the most creative thought and original achievement in American surgery can secure an audience, it will fill a long-felt want, exert a large and important influence, and contribute richly to surgery.

Nowhere in the world have surgeons interested themselves so much in the experimental approach to surgery as here. Yet, no regular agency exists which makes it possible for young men interested in and pursuing the lifelong study of surgery to bring their researches before established surgical bodies. They can, it is true, often obtain an audience before a branch of the American Federated Societies comprising the American Physiological Society, the American Society of Biological Chemists, the American Society for Pharmacology and Experimental Therapeutics, and the American Society for Experimental Pathology. But, why should not these men have the opportunity of an audience from surgeons and why should surgeons be denied the privilege of hearing young men,

the prolonged and complete relaxation of the abdominal wall and abdominal contents which can be obtained with it, it has reduced the mortality and morbidity of our abdominal operative procedures. I feel certain that many of the subtotal and total gastrectomies and resections of the lower end of the esophagus and cardiac end of the stomach would have been made much more difficult and dangerous had it been necessary to perform them under some other type of anesthesia.

I have no desire to agitate for the universal employment of spinal anesthesia in abdominal operations. I do greatly desire to agitate for the training and development of a greater number of anesthetists who are experts in spinal anesthesia of the various types. I am anxious to be certain when we are discussing spinal anesthesia critically that we who are for or against it are discussing it in the same terms. I would epitomize this into the statement that spinal anesthesia, certainly high spinal anesthesia, should never be given except by or under the direction of one experienced and expert in its use. When we are discussing this method of anesthesia and its complications or fatalities without this requirement of expertness and experience, we may unjustly discredit a method when the discredit should properly be assigned to an individual.

—Frank H. Lahey, M.D.

Boston, Mass.

TO THE EDITORS:

In a recent issue of *SURGERY* (pages 282-309, February, 1940), there appeared a review on *Blood Transfusion* by Vary. My purpose in writing is to correct some statements it contains.

In the section on "faulty technique in pretransfusion testing" appear the sentences (page 296): "Isoagglutinins and isoagglutinogens may be absorbed or adsorbed by dissimilar or immunized cells or serum respectively for experimental purposes and the identification of subgroups and abnormal agglutinins. There are two subgroups identifiable as such by especially prepared sera; one of type A, called A_2 ; and one of type AB, called A_2B which are uncommon and so indistinct with the usual typing sera that one is apt to mistype them." The meaning of the former sentence is not clear to the writer. With regard to the subgroups, an understanding of which is required for routine blood grouping, a correct presentation would be as follows. There are two sorts of agglutininogen A, designated as A_1 and A_2 , and these give rise to two subgroups in Group A; namely, A_1 and A_2 , and two subgroups in Group AB, A_1B and A_2B . The agglutininogen A_2 is not uncommon, since in most white populations one-fifth of all Group A individuals belong to Subgroup A_2 and about one-fourth of all Group AB individuals to Subgroup A_2B . The reactions of blood containing agglutininogen A_2 in Group O and Group B sera (containing agglutinin anti-A) are weaker than those of blood containing agglutininogen A_1 , but if high titered grouping sera are used for typing, as they should be, strong reactions are also obtained with bloods of Subgroups A_2 and A_2B .

As for the role of the subgroups in transfusion reactions, the review states: "Unquestionably, unrecognized subgroups account for a small number of serious incompatibility reactions." This is a point of some practical importance, and it may be remarked that, while from theoretical considerations such instances may very possibly occur, no case has yet been reported in which the subgroups of Group A were definitely shown to be responsible for hemolytic reactions. Incidentally the

I feel sure that the differences of opinion as to the value and safety of spinal anesthesia are largely related to the fact that proponents and opponents of the method frequently discuss the subject and evaluate the method without first establishing common criteria. Without the establishment of these common factors, opinions and decisions for or against spinal anesthesia are of little value and are bound to create attitudes which are not basically sound.

One cannot compare the results obtained with spinal anesthesia given by one who is expert in its use with spinal anesthesia given by the surgeon who is to operate and who then turns the patient over to a nurse or to an assistant to watch, or with spinal anesthesia given by one inadequately trained in its use. One cannot compare spinal anesthesia with any other anesthesia without being completely aware of the developments which have taken and are taking place in it—pontocaine, dilute nupercaine, and the as yet unproved but promising continuous spinal anesthesia (Dr. William T. Lemmon). It is wrong to assume that the introduction of drugs into the spinal canal as a method of producing anesthesia is in any way comparable with some of the other methods of anesthesia, for example with that produced by ether. One is a rough and ready, almost foolproof method of obtaining anesthesia; the other, a highly technical method capable of producing great harm unless given by a well-trained person.

Anyone discussing spinal anesthesia, we believe, must accept certain basic facts, one of the most important of which is that, when a spinal anesthesia is given, particularly for an upper abdominal operation, regardless of the expertness of the anesthetist, the anesthesia will occasionally extend to and beyond the desired level and produce paralysis of external respiration. If it has been administered by one experienced and expert in spinal anesthesia and its recent developments, this state will be promptly recognized. The anesthetist will carry the patient on by means of oxygen and the breathing bag until anesthesia ceases and voluntary respiration returns. As has been my own experience more than once, the operator will not know that this condition has existed until the operation is over. Should this occur, however, with a nurse or an inexperienced house officer observing the patient, failure to recognize the true state of affairs and to institute proper measures to meet it can and undoubtedly has resulted in fatalities. This is but a single example of many, evidencing the fact that spinal anesthesia must be given by those expert and experienced in its use.

We have now administered over 10,000 spinal anesthetics. Practically all abdominal operations, high and low, are done in our clinic under spinal anesthesia. There have been no fatalities attributable to spinal anesthesia. There are no patients in whom there exists a neurological complication related to the spinal anesthesia. I have personally performed many of the operations upon those patients to whom the spinal anesthesia has been given and am definitely convinced that, because of

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

SOME CURRENT PROBLEMS OF ANESTHESIA

HENRY K. BEECHER, M.D., BOSTON, MASS.

(From the Anesthesia Service, the Massachusetts General Hospital)

(Continued from the June issue)

ORGANIC EFFECTS

Blood Changes During Anesthesia.—

Blitstein (1937) has made a very long study of physicochemical alterations of the blood after surgical interventions under various anesthetics. It is difficult to evaluate such blood changes when the setup is complicated by surgery. This does not imply that such studies are valueless, but it does mean that it is virtually impossible to estimate their worth unless the reviewer is personally familiar with the controls used and the clinic where they were carried out. In any case, it is dangerous to draw inferences as to the role of the anesthetic from such studies.

Blood Concentration Influenced by Ether and Barbiturates: Many circumstances can effect rather wide variations in the concentration of the several elements in the blood. Bollman, Svirbely, and Mann (1938) point out that the rapidity of the variations in plasma volume caused by withdrawal of water from the tissues to the blood or the loss of fluid from the blood to the tissues is less generally appreciated. They have considered experimentally the influence of ether and amytal anesthesia upon blood concentration in dogs.

Light amytal anesthesia usually produced a definite reduction in the hematocrit value. Typically there was a definite increase in the plasma volume. These changes were of the same relative magnitude, so that the total circulatory blood volume appeared only slightly changed. Following splenectomy there occurred a smaller decrease in the hematocrit values and about the same increase in total plasma volume as occurred in the intact dog.

Light ether anesthesia of normal dogs resulted in an increase in the hematocrit value and a decrease in total plasma volume. There was little if any net change in blood volume. Splenectomized dogs receiving ether anesthesia showed similar changes in blood concentration with the exception that the hematocrit values did not show enough change to indicate an increased volume of cells in the general circulation. Normally a more marked decrease in the plasma volume and in the total circulating blood volume occurred than in the intact animal under similar circumstances.

article by Culbertson and Ratcliffe, cited as a reference for the statement regarding the relation of the subgroups to serious transfusion reactions, deals with quite a different subject.

In the same paragraph (page 296) appears: "The factors responsible for type determination when properly classified into three genotypes, A, B, and R, obey the Mendelian law of inheritance. There are two other factors called M and N which exist, independent of type, and are similarly inherited by assuming an added allelomorphie gene P." The actual facts are as follows: It is generally accepted that the heredity of the four blood groups, O, A, B, and AB, depends upon three allelomorphie genes, A, B, and R, which in combination give rise not to three but to six genotypes; namely, genotype RR, corresponding to Group O; genotypes AA and AR, corresponding to Group A; genotypes BB and BR, corresponding to Group B; and genotype AB, corresponding to Group AB. With regard to the agglutinogens M and N, these are inherited by means of a pair of allelomorphie genes, M and N. The agglutinin P and its corresponding gene P have no connection with the heredity of M and N.

In the section on the early history of transfusion (page 282), Francesca Folli is credited with having performed the first transfusion in animals in 1654. Other writers have credited Francesca Folli with having performed the first transfusion from man to man; but in the article by Mayrhofer, who has made a careful study of this question (Mayrhofer, B.: *Med. Welt*. 12: 473, 1938) it is asserted that Folli never actually carried out a transfusion either in man or in animals, but merely theorized as to the manner in which such transfusions could be done, just like other writers, such as Hieronymus Cardanus and Magnus Pegelius, before him (Scheel, P.: *Die Transfusion des Blutes*, Copenhagen, 1802). According to Zimmerman and Howell, the first authentic transfusion in animals was carried out not by Folli but by Lower in 1665, using dogs as the experimental animal (Zimmerman, L. M., and Howell, K. M.: *History of Blood Transfusion*, *Ann. Med. Hist.* 4: 415, 1932).

Finally, with regard to the discovery of isoagglutination, full credit belongs to Karl Landsteiner, and it was primarily for this important discovery that he was awarded the Nobel Prize in Medicine in 1930, and the Cameron Prize by the University of Edinburgh. As has repeatedly been pointed out (Wiener, A. S.: *J. A. M. A.* 100: 208, 1933; *Blood Groups and Blood Transfusion*, ed. 2, 1939; Ottenberg, R.: *J. Mount Sinai Hosp.* 4: 264, 1937; Coca, A. F.: *J. Immunol.* 20: 263, 1931) and as can clearly be seen by consulting the original article by Shattock (*J. Path. & Bact.* 6: 303, 1900), Shattock's observations did not deal with isoagglutination but with rouleaux formation. In Landsteiner's papers (*Zentralbl. f. Bakt.* 27: 357, 1900; *Wien. klin. Wchnschr.* 14: 1132, 1901), the Groups O, A, B are described; the fourth and rarest group, AB, was discovered not by Jansky but by Decastello and Sturli (*München. med. Wchnschr.* 14: 1132, 1902), the latter a pupil of Landsteiner's who continued the work at Landsteiner's suggestion. The main contribution of Jansky and Moss was that they suggested two different designations of the groups by numbers I, II, III, and IV. In order to avoid confusion these are now replaced by the International Nomenclature by letters O, A, B, and AB in scientific publications, this nomenclature being advocated for general use by the American Medical Association (Report of the Committee on Medicolegal Blood Grouping Tests, *J. A. M. A.* 108: 2138, 1937).

The above remarks are not intended to detract from the value of a review that contains valuable information on a subject which is still in development and of considerable interest for the surgeon.

ALEXANDER S. WIENER, M.D.

Bacteriological and Serological Laboratory, Office of
the Chief Medical Examiner of New York, N. Y.

Interstitial fluid volume as measured in these patients by the thiocyanate method showed an increase of surprisingly great proportions. Either a reduction in the extracellular ions, sodium, and chloride, or an extracellular increase in concentration of the largely intracellular potassium ion, would be expected here. Stewart and Rourke found neither condition and conclude that this apparent increase must be open to question, although it is so large and so constant a finding that it is probably true.

In agreement with the observations of others they found that the concentrations of serum potassium and bicarbonate are significantly reduced.

A striking feature of this study is the extraordinary stability of the composition of the blood, despite the great demands imposed upon the homeostatic mechanisms in the course of anesthesia and operation.

Evipal and Reported Anemia: Dallemagne (1938) continues to state that evipal anesthesia may be followed by a grave degree of anemia.* Beecher (1938) was, however, unable to confirm this observation and found, on the contrary, that, even when a more intensive and more prolonged exposure to evipal was carried out than that employed by Dallemagne, detailed studies of the erythrocyte count, the cell volume, the mean corpuscular volume, the hemoglobin, and the oxygen capacity all failed to show any anemia-producing effects of evipal.

Blood Glutathione: Giuffrè (1939) reports that subcutaneous infiltration with solutions of novocain, pontocaine, and percaine causes a more or less notable diminution of the blood glutathione, less with those of lower toxicity, novocain and pontocaine, and more for percaine.

Carbohydrates: Macintosh and Pratt (1938) have reviewed the subject of carbohydrate metabolism during anesthesia. This is discussed further in the following section on the liver, and in particular in the work of Hrubetz and Blackberg recorded there.

I. A. Lerman (1936) has studied the influence of sodium barbital, chloroform, and ether upon glycemia in dogs. The barbital was administered by mouth. The rate of absorption is too uncertain by this method for use in such a study as this. Tables of data such as are presented in the article are also of little value unless the changes observed are established as significant by statistical methods.

Defandorf (1938) reports that the administration of anesthetic doses of paraldehyde to healthy, fasting dogs produced a small elevation of the blood sugar level. This was greatest during the first hour and averaged 16 mg. per cent. High elevations of blood sugar occurred in poorly nourished animals under paraldehyde anesthesia.

Glycosuria did not occur in normal dogs during paraldehyde anesthesia. Significant quantitative changes in the rate of urine secretion were not observed.

*Study made on dogs.

In a study of the total numbers of erythrocytes and leucocytes per cubic millimeter before and after ether and sodium amytal anesthesia, Higgins and Corwin (1937) have utilized rats and rabbits before and after splenectomy. The blood counts (excepting erythrocytes in rabbits) in the intact animals have been found to be significantly lower under amytal than under ether anesthesia. Following removal of the spleen, they conclude that this organ is not an important site for sequestration of erythrocytes from the peripheral blood of rats and rabbits under sodium amytal anesthesia. They conclude further that under sodium amytal the spleen plays an important role in the sequestration of leucocytes in rats but not in rabbits. Increase in plasma volume dilutes the circulating blood elements under sodium amytal anesthesia, resulting in lower counts. The increase in plasma may also account for the distended spleen encountered under the barbiturate.

Hamlin and Gregersen (1939) report that the intravenous injection of nembutal to produce anesthesia causes a 10 per cent increase in plasma volume in normal cats, but an increase of only 2 per cent or less in sympathetomized animals.

McAllister (1938), in studying the effect of ether anesthesia upon the volume of plasma and extracellular fluid (Gregersen's spectrophotometric method), found in twenty-three experiments on dogs that one hour of anesthesia caused an average decrease in plasma volume of 11 per cent. Calculating the decrease in plasma volume from the rise in concentration of the serum proteins, the fluid loss averaged 9.3 per cent. He found further that the hematocrit rise was about twice that which could be accounted for by the decrease in plasma volume. Following splenectomy, this discrepancy became less.

Few observations have been made of the changes in body fluid of patients which result from anesthesia (cf. McAllister on animals), although the changes produced in concentration of many of the components of the blood have been considered at length. While studies of patients undergoing operation and anesthesia are open to certain obvious criticisms, the findings recorded by Stewart and Rourke (1938) are nevertheless of much interest. Studying sixteen patients who underwent ether anesthesia and surgical operation, they find that a notable reduction in blood volume occurs without appreciable change in the physical or chemical character of the blood (see below). The average reduction in volume was 13.4 per cent. Concentration of the structurally important components of blood plasma—protein, sodium, and chloride—were accurately maintained. This stability makes it evident that the reduction in blood volume is not due to dehydration. The blood loss occurring in the course of the operation was measured in thirteen of the cases and was not adequate to account for the volume decrease.

Weisel, Youmans, and Cassels (1938) have studied in dogs the effects of morphine, scopolamine, and cyclopropane upon the motor functions of the intestine, considering separately tonus and nonpropulsive and propulsive movements, since these may be affected unequally and in opposite directions. Morphine (1 mg. per kilogram), they find, produces a rise in tonus and an increase in both propulsive and nonpropulsive intestinal movements. This increase is followed in from ten to twenty minutes by a period during which propulsive movements are nearly absent, although the tonus remains high and the nonpropulsive movements are still above normal amplitude. These findings are in agreement with those of other investigators.

Scopolamine (gr. $\frac{1}{50}$ to $\frac{1}{100}$ per dog) quickly produces complete inhibition of movements and lowered tonus.

Morphine and scopolamine together produce an effect about the same as morphine alone.

Cyclopropane anesthesia produces a decrease in intestinal tonus and inhibits all types of movements in unpremedicated dogs. In deep anesthesia the inhibition is complete. When premedication with morphine and scopolamine has been used, cyclopropane anesthesia does not lower the high tonus of the bowel, but it partially inhibits nonpropulsive movements. Propulsive movements are absent.

Termination of cyclopropane anesthesia is followed by an immediate return of the nonpropulsive movements to the preanesthetic level. Recovery of tonus is rapid, while recovery of propulsive movements may occur at once or may require several hours in premedicated or unpremedicated animals.

While Peoples and Phatak (1935) have shown that isolated rabbit's intestine in cyclopropane and oxygen increases in tonus, it seemed desirable to repeat this in the intact animal. Burstein (1938, a), using dogs with Thiry-Vella fistulas of the jejunum or ileum, observed that cyclopropane causes an increase of both intestinal contractions and tone in the first two planes of third-stage anesthesia. In the lower planes of this stage, contractions are inhibited, but tone is maintained. It is interesting to compare this with ether which causes an abolition of the contractions in all planes of the third stage. (See above reports.)

Sleeth and Van Liere (1938) have carried out in dogs a comparative study of the effects of various anesthetic agents upon the emptying time of the stomach. Using a standard barium meal and making observations with the fluoroscope, they found under all agents a prolongation of the emptying time: chloroform by 64 per cent, ether by 40 per cent, and ethylene, cyclopropane, and divinyl ether by about 7 per cent. They also report a 15 per cent increase for nitrous oxide. This is scarcely worth inclusion, for only 5 per cent oxygen was administered with the nitrous oxide. It represents the effect of nitrous

Blood Ascorbic Acid: It has been stated previously by Ecker, Pillemer, and Wertheimer that a close parallelism between complement activity and ascorbic acid content is to be found in guinea pig sera. In the present paper (1938) they provide data showing that a rise in ascorbic acid content of guinea pig serum occurs after thirty minutes of ether anesthesia; yet no marked changes in complement titers were observed. Zilva (1935) found that when l-ascorbic acid was injected into etherized guinea pigs the urinary excretion of the l-ascorbic acid was increased. Bowman and Muntwyler (1935) have found that the urinary excretion of ascorbic acid in the dog following ether anesthesia is increased ten- or fifteenfold.

Kasahara and Gammo (1938) report that the vitamin C content of cerebrospinal fluid is not essentially lowered by ether and chloroform anesthesia in monkeys and rabbits.

The Gastrointestinal Tract.—

Oettel (1935) has made the following observations on the influence of anesthesia and laparotomy on the motility of small intestines. In the normal small intestine of the dog it was shown that under general anesthesia (chloroform, ether, evipan, pernocton, chloralose, avertin, urethane, paraldehyde, chlorotone) the intestines are also anesthetized (paralysis of tonus until a resting position in "diastole" is assured).

Acetylene does not paralyze the intestine of the fistulous dog; even in deep acetylene anesthesia, the intestine goes on working normally.

Morphine, in unanesthetized fistulous dogs, in contrast to the true anesthetics, never causes a paralysis of tonus, even in stupefying doses (about 5 mg. per kilogram), but always an increase in tonus until a spasm lasting for hours occurs (position at rest in "systole").

The movements of the intestine registered under anesthesia after opening the abdominal cavity and cutting the intestine are distinguishable qualitatively and quantitatively from the normal intestinal activity. As a paralysis of the intestine appears after laparotomy even under acetylene anesthesia, the injury to the intestinal motility is dependent upon the operative interference.

The small intestine, entirely paralyzed by anesthesia and operation, regains its ability of rhythmic movement by subcutaneous injection of morphine. In a laparotomy under morphine anesthesia, movements of the intestine can be registered accordingly, which correspond in their main type to the normal activity of the intestine, but are characterized by gradual increase of tonus (typical effect of morphine).

The movements of the intestine appearing after the death of the animal are entirely different from the normal intestinal motility.

Conclusions regarding intestinal motility and the action of substances on the intestine in situ can be drawn only with great reservation from acute experiments in an anesthetized, laparotomized animal.

of the patient, etc. Complicating these uncertainties is the possibility that damage present may have been produced by inadequate oxygen intake, by circulatory derangements, by shock, and so on. In such a confusing situation "negative" findings prove little, and "positive" findings must be interpreted guardedly. At the present time the tests probably used most often in suspected liver damage in the presence of jaundice are the icterus index, the van den Bergh test, and the galactose tolerance test, while in the nonjaundiced patients the bilirubin and bromsulphalein tests are often used. Some simplification of these problems is necessary before any attack can be made conveniently upon them. Coleman (1938), as others had before him (Bourne and Raginsky), decided that the bromsulphalein excretion test was worth employing. In using only 100 cases covering six anesthesia combinations, his data are open to the criticism of inadequacy; however, it is probably fair to draw some inferences from the forty-nine patients who received nitrous oxide-oxygen-ether, the twenty-seven who received nitrous oxide-oxygen, the thirteen who received avertin, and the eight who received spinal anesthesia. He finds in man that avertin produces hepatic damage in a higher percentage of cases and to a greater degree than nitrous oxide-oxygen-ether, than nitrous oxide and oxygen, and than spinal anesthesia, and that the liver is slower in recuperating from damage produced by avertin than from the others. Interestingly enough, he finds nitrous oxide-oxygen less damaging to the liver than spinal anesthesia. (Data on the blood pressures encountered would be of interest.) Whatever the anesthetic agent used, the longer the duration of use, the greater the chance of liver damage. The older the patient, the greater his chance of hepatic damage will be.

Reynolds, Schenken, and Veal (1938) report a high percentage of focal liver necrosis in mice anesthetized by pentothal; this was not so with evipal or amytal.

Forbes, Neale, and Scherer (1936) describe a liver concentrate which, on injection into rats, protects them to a great extent against carbon tetrachloride and chloroform poisoning. What the substance is or how it protects is not known. It is believed not to be choline, glucose, or the pernicious anemia factor.

The suggestion that low blood amylase is associated with liver damage has led Cajori and Vars (1938) to produce liver damage in dogs with chloroform anesthesia and to observe simultaneous changes in blood amylase. They found that the amount of decrease of serum amylase was related to: (1) duration of the anesthetic; (2) elapsed time following administration of the anesthetic; (3) whether the chloroform was volatilized with air or oxygen (greater decrease when air was used); (4) degree of liver damage as revealed histologically. From these facts and other evidence obtained it seems probable, although by no means certain, that the low serum amylase level found was the result of changes in the liver induced by chloroform.

oxide anesthesia plus severe anoxia. This paper contains some indication of the probable reasons for the more frequent postoperative gastrointestinal disturbances following ether, for example, than following cyclopropane or ethylene.

A marked inhibition of the gut during anesthesia has already been described. Emerson (1936) has shown in a study on rats that ether anesthesia increases significantly the reduction processes taking place in the rats' intestines. These reduction processes, following one hour of "surgical" ether anesthesia, reach a peak with the fecal sample taken six hours after induction of anesthesia. Some augmentation over those of untreated controls is shown up to the eighteenth hour following anesthesia. It is doubtful if one can draw any analogies in man, for the definite and regular biochemical effects of the functional disturbance in rats have not been identified in man.

Burstein (1938, b) has studied the effect of divinyl oxide on intestinal activity in vivo. He recalls that Peoples and Phatak have observed that the tone of an isolated intestinal segment is increased by divinyl oxide; whereas, in the present study Burstein finds, contrary to the in vitro studies, that all animals (six dogs) showed effects identical to those obtained with ether (diethyl)—diminished muscular tone and complete inhibition of intestinal contractions during all planes of surgical anesthesia.

Ethyl alcohol diminishes the tone and peristalsis of the human stomach. Barlow (1936) found this true for all doses studied. Interestingly enough, he found that whisky containing equivalent amounts of alcohol actually increased gastric tone and motility, and it was only after relatively large doses of whisky that the depression characteristic of alcohol appeared.

Asteriades (1938) recounts several cases of postoperative ileus successfully treated by spinal anesthesia.

In regard to gastrointestinal disturbances, Taylor, Bennett, and Waters (1937) find that "total nausea and emesis" under cyclopropane occur in 28.7 per cent of the cases, whereas under ether the figure is 40.6 per cent. They find the nausea to be less severe and of shorter duration under cyclopropane than under ether.

The Liver.—

In any determination of the effects of anesthesia upon hepatic function a number of considerations are inescapable. Is the liver damaged by the operative intervention, for example? The operative factor can be controlled with some degree of completeness by a large series of similar cases under various anesthetic agents. Considerable doubt can be raised fairly of whether measurement of one of the liver's numerous functions gives a useful picture of damage produced by the anesthetic agent. This is aside from reasonable questions of sensitivity of the tests used, duration of anesthesia, age and condition

They found divinyl ether to be an unsatisfactory anesthetic agent for use with dogs. The animals were too often either about to awake or about to die. The safe anesthesia zone appeared to be narrow, narrower than for man, they conclude. When death occurred following the use of too great a concentration of the drug, it was apparently due to respiratory failure closely followed by cardiac failure.

Ravdin, Vars, Goldschmidt, and Klingensmith (1938), in continuing their studies of anesthesia and liver damage, have taken up the problems of whether the use of oxygen as the volatilizing agent in chloroform anesthesia has a sparing effect upon liver glycogen, or whether it modifies or prevents fatty infiltration of the liver and whether it influences the level to which the blood sugar might rise during anesthesia and the rapidity of the fall following anesthesia. Dogs and white rats were used in the studies.

They report that during chloroform anesthesia the blood sugar level is the same whether air or oxygen is used in volatilizing the agent, although, of course, when anoxia exists great increase occurs in the blood sugar level. Rise in blood sugar during anesthesia was not proportional to the original glycogen concentration.

Ravdin (1939), in summarizing earlier work by himself and his associates, says that adequate oxygen in the inspired air during anesthesia will have almost as much protecting action on the liver as a high carbohydrate intake.

Influence of Diet on the Action of Anesthetic Agents, With Some Remarks on Hepatic Function.—

There is nothing new in the demonstration that diet can influence the physiologic action of drugs. Many examples of this can be recalled. For instance, there is the work of Salant and Swanson (1918). In studying the toxicity of sodium tartrate, they used cats, rabbits, and rats and found that diets rich in sugar were efficacious in decreasing the toxicity of the tartrate. The toxicity of sodium tartrate was most marked on a diet of oats, hay, and cabbage. Resistance to the tartrates was much higher when the animals were fed a diet of carrot leaves. Then, there is the observation of Blatherwick and his associates (1924) who presented data to show that rabbits fed on a base-forming diet are less resistant to insulin than animals fed on an acid-forming diet. This observation was confirmed by Geiger and Kropf (Hjort et al. [1939]).

It is of some interest to consider the accounts of the influence of diet on the action of anesthetic agents. Benecke (Hjort) found that the toxicity of avertin was apparently uninfluenced by unbalanced diets. This is somewhat surprising when one considers the similarities of the toxic effects of avertin and chloroform, and surprising in the light of the work of Ravdin and his associates (to be described in some detail below) and others regarding the influence of diet on chloroform poisoning.

Liver esterase was found to be decreased in livers made severely necrotic by chloroform.

Bourne, McDowell, and Whyte (1937) recount earlier work of Bourne and Raginsky in which the following conclusions in regard to vinyl ether were made (the liver function was tested with bromsulphalein dye):

1. Vinyl ether anesthesia in normal dogs does not appreciably alter liver function.
2. If cyanosis occurs during this anesthesia, liver necrosis may result.
3. Vinyl ether anesthesia neither enhances previous liver damage nor delays recovery from it.
4. Vinyl ether anesthesia does not have a greater effect upon the liver function of starved dogs than it does in normal dogs.

They describe Molitor's work (personal communication and apparently previously unpublished). Molitor placed a cannula in the bile duct, and, with a drop recorder to indicate changes in rate of flow, he proceeded to measure and weigh the bile formed. This was reinjected into the duodenum. A control animal showed a pronounced decrease in bile flow in the first hour and slow and gradual increase in the next two hours. Under chloroform an immediate decrease in bile flow occurs; this persists even after the anesthesia is withdrawn. Under ethyl ether there was a slight initial decrease and a subsequent increase in bile flow as in the control animal. Under vinyl ether there was no change in bile flow, even with two hours of profound anesthesia. With 95 per cent nitrous oxide and 5 per cent oxygen there was a prompt drop in bile flow, almost complete cessation. This was then changed to 80 per cent nitrous oxide and 5 per cent oxygen + vinyl ether to produce deep anesthesia, and the bile flow was resumed, reaching its normal rate in five minutes.

Oxygen and Hepatic Function During Anesthesia.—

An interesting historical review of the relationship of anesthetic agents to liver function is presented by Bourne (1936). His concluding remarks are of interest here: "It can be said that, with the exception of cyclopropane, all anesthetics may cause some impairment of liver function. But this should not be taken too seriously, except in the case of chloroform. . . ." The protective action of adequate oxygen is well established. Oxygen shortage may cause irreparable liver damage.

After a study of the effects of divinyl ether anesthesia in dogs, Bourne and Raginsky (1935) conclude that the agent does not alter liver function appreciably in dogs that are normal, unless the anesthesia is accompanied by anoxia, in which case liver damage occurs.*

*See Ravdin et al.

that variations in diet of experimental animals may be responsible for great variations in sleeping time, hence the necessity for controlling this factor in anesthesia studies. Not only were significant differences obtained in the minimum hypnotic dose (unsymmetrical *n*-propyl-*o*-tolyl urea) but in the minimum lethal dose as well.

One cannot escape the obvious implication of the above studies that variations in diet may be responsible, at least in part, for the puzzling and at times dangerous variations in response of patients to the clinical use of barbiturates.

There is no need for reviewing at this time the great number of well-known studies on the influence of diet on the development of chloroform poisoning in animals subjected to anesthesia with that agent. The recent interesting studies of Ravdin and his associates will, however, be considered below.

Blackberg and Hrubetz (1936) have found, in a study of the factors which influence pentobarbital (nembutal) anesthesia, that glucose by vein does not materially shorten the duration of anesthesia, whereas fasting for twenty-four hours materially increases the period of anesthesia. No correlation between blood sugar levels and susceptibility could be demonstrated. The blood sugar level at the time of greatest depression from the agent continued at the initial level until the time of recovery, when a definite drop occurred.

Blackberg and Hrubetz (1937) report that fasting for twenty-four hours increases the susceptibility of rabbits to pentothal. The duration of anesthesia is lengthened. No correlation was found between the blood sugar level and the susceptibility to the drug.

One of the well-known hazards of the use of barbiturates is their variability of action. The factors underlying this variability are not at all clear. It is known that fasting increases susceptibility to barbiturate action, and so the findings of Hrubetz and Blackberg (1938) are of considerable interest. They found that, although animals (rabbits) deprived of food for twenty-four hours showed an increased susceptibility to the anesthetic, they could not correlate this with the blood sugar levels. Nembutal and amytal produce no change in blood sugar levels at the time of deep anesthesia. Phenobarbital causes none in the first hour. Pentothal and seconal bring about a rise in the first hour. In general, the agents produce a significant fall in blood sugar level at the time of recovery from anesthesia. Since lowering of the blood sugar level does not explain the increased drug effects, they investigated liver function and carbohydrate mobilization.

With each of the barbiturates studied (nembutal, pentothal, seconal, amytal, and phenobarbital) they found a marked depression in the glycogenolytic power of the liver as shown by the absence of or diminution in the rise in blood sugar after epinephrine. The short-acting

Continuing on the same theme, it is interesting to find that Cutler (1932), while not able to demonstrate any consistent differences in the amount of liver damage produced by carbon tetrachloride in dogs on various diets, was able to show that the severity of the symptoms and the number of the deaths secondary to the liver damage could be affected profoundly by the diet, a high calcium diet affording considerable protection.

Widmark (Hjort et al. [1939]) found that the ethyl alcohol level of the blood of fasting dogs was lower than it otherwise was when the fasting animals received various amino acids with the alcohol, by mouth. He also observed a similar effect when proteins or certain acids were given with the alcohol; water, fat, and carbohydrate were ineffective.

A notable increase in sensitivity of rabbits to cocaine was accomplished by Nedzel (1934) when the animals were placed on an acid-forming diet (urine reactions) over that found when they were living on an alkali-forming or mixed diet. He (1935) has described experiments which suggest that rabbits are more sensitive to ethyl hydrocupreine hydrochloride poisoning when on an acid-forming diet. In considering the influence of diet upon the action of phenobarbital sodium in rabbits, Nedzel (1937) found evidence that the animals on a diet producing an acid urine undergo longer general anesthesia than those on a mixed diet (urine nearly neutral).

Hjort, deBeer, and Fassett (1939) have studied the effect of diet in albino mice upon the anesthetic qualities of several hypnotics (n-symmetrical n-propyl-o-tolyl urea, ethyl-o-ethylphenyl urea, and sodium ethyl [1-methyl-butyl] barbiturate). Remarkable variations in sleeping time were elicited by altering the diets.

TABLE VI

| DIET | NUMBER OF MICE USED | MEAN SLEEPING TIME (MINUTES) |
|---|------------------------|---------------------------------|
| 1. Whole grain diet | 30 | 85.6 |
| 2. Grain flour diet | 59 | 93.2 |
| 3. Purina dog chow | 30 | 19.3 |
| 4. High carbohydrate diet | 57 | 48.5 |
| 5. High protein diet | 57 | 34.9 |
| 6. Grain diet with cod-liver oil | 58 | 81.4 |
| 7. Grain diet with cod-liver oil and ascorbic acid | 58 | 91.5 |
| 8. Grain and milk diet | 57 | 55.8 |

They were unable to determine the cause of these variations in sleeping time. Interestingly enough, they did not appear to be related to acid-forming or base-forming elements, for the diets used tended to be acid-forming. Reasons are presented why the variations cannot be explained on the basis of high protein or high carbohydrate contents. Whatever the explanation may be for the variations in sleeping time, the practical point to be gained from these studies is

that variations in diet of experimental animals may be responsible for great variations in sleeping time, hence the necessity for controlling this factor in anesthesia studies. Not only were significant differences obtained in the minimum hypnotic dose (unsymmetrical *n*-propyl-*o*-tolyl urea) but in the minimum lethal dose as well.

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barbiturates are believed to be largely detoxified in the liver and accordingly might be expected to influence the glycogenolytic function of that organ; however, phenobarbital eliminated by the kidneys likewise depresses liver function. These findings strongly suggest that all barbiturates, however eliminated, produce a transient impairment of liver function.

Ravdin, Vars, Goldschmidt, and Klingensmith (1938) believe that the prolonged hyperglycemia observed following termination of chloroform anesthesia is due to damage of liver cells (dogs, white rats) by the anesthetic agent. Liver glycogen content was found to be reduced steadily during the anesthesia period. About 35 per cent of the liver glycogen was lost during a two-hour period of anesthesia; however, glycogen continues to disappear from the liver so that 94 per cent of it has been lost twenty-four hours after anesthetization. With the fall in liver glycogen concentration, the fatty acid concentration of the liver increases. When glucose is administered following anesthetization, a simultaneous increase in liver glycogen and liver fat occurs. This is evidence against the existence of a reciprocal relationship between these substances as reported by others.

The influence of foodstuffs upon the susceptibility of the liver to injury by chloroform and the probable mechanism of their action have been considered in rats by Goldschmidt, Vars, and Ravdin (1939). They find that the incidence and severity of damage to the hepatic cells increases progressively with an increase in the concentration of lipids in the liver. This is quite independent of the content of glycogen in the liver at the beginning of the anesthesia; but it may be modified by the protein content of the ration. The chief reason for the protection of the liver against injury, following a diet high in carbohydrate content, is probably the reduction in the lipid content of the liver which results from such a diet. Under certain circumstances, for example, inanition, the administration of carbohydrate may protect the liver by its protein-sparing action. Ravdin and his associates find no evidence that the depletion of hepatic glycogen by chloroform is associated with the metabolic requirements of the liver. They consider that this depletion is probably a manifestation of a effect of the toxic agent.

A high protein diet preceding chloroform anesthesia greatly reduces the incidence of hepatic cellular necrosis, even in livers which contain a high lipid content, and because of this, notwithstanding a severe attack by the chloroform.

Vars, Goldschmidt, and Ravdin (Ravdin [1939]) present further evidence that the high carbohydrate intake acts in several ways in protecting against chloroform poisoning:

1. Liver glycogen displaces liver fat. (Fat concentrates the anesthetic agent by absorption, and the agent produces necrosis by direct cellular damage.)

2. The high carbohydrate intake spares the reserve stores of protein in the liver. (These are important in protecting against hepatotoxins, such as chloroform.)

Adequate protein, as well as abundant carbohydrate, in the diet is important. Food by mouth is essential if intravenous glucose is to increase the quantity of carbohydrate stored in the liver, the authors state.

Liver Damage and Sleeping Time Under Barbiturates.—

Cameron (1939) recalls the work of Pratt and his associates (1932, 1933), finding that dogs given nembutal twenty-four hours after prolonged chloroform anesthesia sleep much longer than "normal" animals. No such effect was found for barbital. Koppanyi and his associates (1936) confirmed this work in cats and dogs. These workers, however, found prolonged sleep with barbital. They suggested that chloroform injures the nerve cells, making them more susceptible to the barbiturates. Cameron and deSaram (1939) produced liver damage by means of carbon tetrachloride. Following this, nembutal and evipan were found to produce abnormally prolonged sleeping times, although in the case of the slow-acting agents, medinal and luminal, no prolongation was observed.

Progressive liver damage was produced in rats by giving twice-weekly doses of carbon tetrachloride subcutaneously, with the results shown in Table VII:

TABLE VII

| DURATION OF LIVER DAMAGE | NUMBER OF RATS | MEAN DURATION OF SLEEP IN MINUTES AFTER STANDARD DOSE OF NEMBUTAL.* | MORTALITY FOLLOWING STANDARD DOSE OF NEMBUTAL |
|--|----------------|---|---|
| Normal | 55 | 102 \pm 4 | 0 |
| One month CCl ₄ intoxication | 20 | 148 \pm 14 | 12.5% |
| Two months CCl ₄ intoxication | 18 | 208 \pm 10 | 28.0% |
| Three months CCl ₄ intoxication | 12 | 249 \pm 22 | 58.0% |

*Forty mg. per kilogram of body weight, given subcutaneously.

After one month of CCl₄ intoxication, the liver shows only very slight alteration either grossly or microscopically, yet a significant prolongation of sleeping time occurs, and lethal effects occur with a dose below the normal minimum lethal dose.

In other experiments they found that chilling increased the mortality.

Some Examples of the Use of Anesthetic Agents in Studying Physiologic Processes.—

Acquired Resistances of Fixed Tissue Cells: MacNider (1938) reviews his work extending over thirty years on the acquired resistance of fixed cells (liver, kidney) that develops as a process of cell metaplasia secondary to tissue injury (uranium, chloroform). These studies

are of interest here simply as an example of how anesthetics, even their toxic effects, can be utilized in unravelling the processes of physiology and pathology.

Blood Clotting: Smith, Warner, and Brinkhous (1937) present another example of the use of an anesthetic agent (chloroform) in the study of liver function. In severe liver damage by chloroform, disturbance of blood clotting occurs. Clots can form, but they are flabby and ineffectual in controlling hemorrhage from minor incisions. The bleeding tendency is due to a deficiency in fibrinogen and also to a great fall in plasma prothrombin. Smith and his associates (*loc. cit.*) have demonstrated (in dogs) that the prothrombin is more labile than the fibrinogen. When the chloroform dosage is small, the prothrombin level falls much more markedly than the fibrinogen level. By using repeated small doses of chloroform, these two clotting factors can be dissociated, the fibrinogen level remaining unaffected, while a great fall in the prothrombin level occurs. The relation of liver injury to the plasma prothrombin level demonstrates that the liver is concerned in the manufacture of prothrombin. Chloroform damage appears to interfere more easily with prothrombin formation than with fibrinogen formation.

Renal Function.—

The effects of the common anesthetic agents on normal kidney function have been studied on several occasions. In this regard, the recent paper of Orth and Stutzman (1938) is of considerable interest. Since urea is the chief product of excretion in the urine and since both tubules and glomeruli are involved in filtration and reabsorption, urea clearance determination would appear to give an index of the action of anesthetic agents on the kidneys if damage occurred. It is well known that slight fluctuations in clearance values may occur and represent normal variation in kidney function. Sixty- to seventy-five-minute periods of "surgical" anesthesia with cyclopropane, ether, or chloroform were carried out in dogs at about weekly intervals for many weeks. The results indicate that none of the three anesthetic agents studied interferes with kidney function, as determined by urea clearance. Repeated collections of twenty-four-hour urine samples following each anesthetic agent also showed normal volumes. Microscopic examination showed "slight casts, leucocytes, and occasional erythrocytes." A slight albuminuria was present after ether but cleared within a few days. The authors did not encounter this after cyclopropane or chloroform. They have never found glycosuria.

It has been shown by a number of workers that the rate of secretion of the urine is diminished under sodium isoamylethyl barbiturate. It has also been shown that under this agent dilution of the blood occurs. Gouaux and his co-workers (1937) have studied the effect of this anesthetic agent in fifty dogs, and they find that there is no serious interference with kidney function, as measured by the urea excretion.

Smith, Rovenstine, and their associates (1939) have studied the circulation of the kidney under spinal anesthesia in twenty-one unoperated subjects. Anesthesia to levels above those at which the efferent sympathetic paths to the kidneys emerge from the cord does not produce renal hyperemia, nor any consistent effect upon renal circulation. They conclude "that the tone of the renal arterioles is normally maintained by autonomous, intrinsic activity of the peripheral vascular apparatus and is not dependent upon tonic activity of the central nervous system."

In 1935, Zilva presented evidence that, when compounds of the ascorbic acid series were injected into guinea pigs previously depleted of vitamin C, only the antiscorbutically active members were "fixed" by their tissues. There was, furthermore, some indication that a quantitative relationship existed between degree of activity and quantity "fixed" by the tissues. The amounts of the compounds excreted by the kidneys varied inversely with their antiscorbutic activity. When ether anesthesia was used to facilitate the intravenous injection, the quantity of l-ascorbic acid excreted in the urine increased (doubled) over that excreted in the urine when no anesthesia or procaine local anesthesia was employed. When the several compounds were considered, the influence of the general anesthesia became less as the activity of the antiscorbutic compound diminished.

Kolb and Langworthy (1938) have carried out a comparative study of the effects of barbiturates, ether, and bulbocapnine upon micturition.

Suprarenals.—

Knoefel (1936) has pointed out that many of the undesirable side effects of ether and chloroform anesthesia resemble effects produced by epinephrine and has suggested that a major cause of these side effects is an increased output of adrenin from the suprarenals as a result of stimulation of the hypothalamic "sympathetic center" and increased stimuli through the thoracolumbar system.

Emerson (1938) has pointed out that test of Knoefel's hypothesis should be based upon direct examination of the adrenin content of the suprarenals rather than upon indirect biochemical evidence. Emerson has made such a test and reports (1938) a significant decrease in the amount of adrenin found in the suprarenals of cats anesthetized with ether for thirty minutes, but this was not so after divinyl ether. The decrease did not occur under ether if barbiturate premedication was used.

An increased outpouring of adrenin during anesthesia may be due to (1) excitement during induction or recovery or (2) continued stimulation of the "sympathetic center" or the splanchnics during deep anesthesia. It is possible, as Emerson recognizes, that his results could be criticized justifiably on the basis that longer, stormier inductions under ether than under divinyl ether account for the findings. He attempted to correct for this by the deliberate use of slow inductions under divinyl ether.

Skeletal Muscle Tonus.—

Muscle tonus is a slight elastic pull of muscles which, it has been suggested, is influenced to some extent via the sympathetic nervous system; however, the chief impulses responsible for it come through the motor nerves which control active movements. Muscular tonus is under the active control of the motor centers in the spinal cord. These centers are influenced by reflexes from the skin and muscles and by the higher centers. Oxygen and CO₂ contents of the blood also greatly affect tonus.

Strychnine increases the activity of the spinal nerve centers and increases tonus. Ether (early) increases muscular tonus. Henderson (1937) explains this by saying that the inhibiting influence of higher centers is eliminated and the lower centers become more active. In full anesthesia the activity of the motor centers themselves is diminished, and tonus is lessened or abolished. The muscles relax and become flaccid.

The above is widely accepted. Henderson reports:

1. Tonus induces a pressure within a muscle.
2. This pressure forces the blood onward toward the heart. With low tonus the blood tends to stagnate in the capillaries. With high tonus the flow onward is promoted.

He attributes to low muscle tonus postoperative pulmonary complications (high diaphragm, etc.) as well as shock.

SPECIAL FIELDS

Peridural Anesthesia.—

Tuohy (1938) describes how Pagés in 1921 and Dogliotti in 1933 independently worked out a method of producing segmental or localized anesthesia by injecting a local anesthetic agent into the peridural space. In this space the anesthetic acts upon extradural portions of the spinal nerves, upon the spinal ganglia, and upon paravertebral sympathetic nerves. Usually from 30 to 40 c.c. of a 2 per cent procaine hydrochloride solution are injected; segmental peridural anesthesia then lasts from one to two hours. The chief advantages of this method, as stated by Dogliotti (summarized from Tuohy), are that (1) there is no danger of diffusion of the anesthetic toward bulbar centers; (2) anesthesia is reduced to a very limited segment of the body; (3) there is less fall in blood pressure than that occasioned by subarachnoid injection; (4) there is less nausea and vomiting than occurs under spinal anesthesia; (5) there is an incidence of "lumbar puncture headache" of less than 1 per cent; (6) in debilitated patients a greater margin of safety is obtained than with subarachnoid block.

As disadvantages, Tuohy lists failure to obtain adequate anesthesia in the proper region in some cases and considerable delay in obtaining anesthesia. Perhaps Tuohy considered it too obvious to mention in the outline referred to, but it seems to this reviewer that one should include the hazard of the needle's accidentally puncturing the dura

and arachnoid. After the injection has been well started, it is difficult, if not impossible, to determine whether one is in the peri- or subdural (subarachnoid) space; the two chief tests which indicate the peridural space can no longer be elicited; the negative pressure is no longer present and injected fluid can be aspirated. More than one able anesthetist can testify that this hazard is a practical one. Such large quantities of procaine are used in the peridural technique that, when an accident occurs and these are injected into the subarachnoid space, an extremely serious situation results.

Odom (1936) uses pontocaine and procaine combined in peridural anesthesia, obtaining anesthesia which lasts from one and one-half to two hours. He has described in detail the anatomic background and the technique employed to produce peridural anesthesia.

The Rectal Use of Evipal.—

The rectal use of evipal has been recommended by a surprisingly great number of writers: Gwathmey (1936, 1937, 1939), McNellis (1937), Hogan (1937), Soresi (1937), Harrison and Dunphy (1938), Meana and d'Accinni (1938), Weinstein (1938), and Jones (1938).

There are two main routes of administration for nonvolatile agents for general anesthesia—the veins and the rectum. Some agents, such as avertin, can be introduced only through the rectum. But in the case of the barbiturates, many can be introduced directly into the blood stream. The recommendations of these papers, that the barbiturates be introduced rectally, raise the question of the relative controllability of these two routes of administration.

Several points are pertinent to such a consideration:

1. Once an agent is placed in the rectum it is nearly impossible to recover it after it begins to exert its normal action or to give toxic effects. While high colonic enemas may be tried in an endeavor to wash it out, the fact is that such action may sweep the offending agent higher in the bowel and allow even more rapid absorption with greater toxic effects to follow.

2. Even though a solution of given volume may be injected into the rectum at a standard speed, it is impossible to say to what height it will travel up the bowel. There are a number of reasons for this. There is no need to point out how uncertain cleansing of the bowel may be as a result of routine enemas. The height to which an anesthetic agent will rise on being placed in the rectum is determined in large part by the fecal content of the bowel. Other factors active in regulating height (and impossible of accurate evaluation) are tone of the bowel, peristalsis, and anatomic anomalies. Using a dilute barium solution under exactly the same conditions as avertin is used, Sebening found on roentgenographic examination that in two patients the entire colon including the cecum was filled; in two the midascending colon was reached; in four the hepatic flexure was attained; and in

four the midtransverse colon, in seven the splenic flexure, and in one patient only the rectosigmoid junction was reached.

3. It is well known that the toxicity of the nonvolatile anesthetic agents depends to a great degree upon their rate of absorption. With some of the agents, as with sodium barbital, while the blood level is rising as a result of absorption, it may be counterbalanced by excretion through the kidney and a safe blood level may thus be maintained. In other cases, as with the fast-acting barbiturate, evipal, a safe blood level depends in great part upon liver destruction concomitant with absorption. An abnormally rapid rise in the absorption rate, however, easily upsets the balance experience has taught is safe, and serious toxic effects follow. The higher agents travel up the bowel, the more rapidly they will be absorbed.

4. The following statement, then, seems to be a reasonable one. If we cannot efficiently remove an agent once it is placed in the rectum, if we cannot control the height to which a solution injected into the bowel will rise, then it follows that we cannot control the rate of absorption. In other words, we cannot accurately control the toxicity of nonvolatile agents used rectally. If an agent can be used intravenously there is no reason to resort to the relatively inaccurate and unsafe rectal route. One wonders if the defenders of the rectal route of administration of the barbiturates are prepared to claim that there is any magic in the *route* of absorption. The implication is inescapable in some of the papers referred to that rectal administration prolongs the action of the drug! The rate of administration can be precisely controlled through intravenous drip methods, and if toxic signs appear, the administration can be curtailed immediately. It seems evident that such a method is more desirable than one which cannot be controlled precisely. (Beecher, 1939.)

Also pertinent to this review is the following discussion of the article by Werner, Pratt, and Tatum (1937).

When each of several agents is destroyed by the body at a differing rate, route of administration must loom large in considering dosage. For example, these workers have shown that the order of decreasing toxicity of a number of barbiturates administered by vein is not the same as the order of decreasing toxicity by rectum or by gastric tube.

When the minimum lethal dose ratio (intravenous to oral administration, I:O) is compared for a number of barbiturates with the duration of action, it also becomes plain that a high M.L.D. ratio is associated with brief action when administered intravenously. To put it another way, as duration of action increases from one compound to another, the toxicity ratio decreases. A high ratio (I:O) indicates that detoxication occurs rapidly. The studies just described were based upon values found in rabbits, and they cannot be casually transferred to man. It is likely, however, that the principle would apply

TABLE VIII

COMPARISON OF THE M.L.D. RATIO TO DURATION OF ACTION

| AGENT | M.L.D. RATIO* 1:0 | DURATION IN MINUTES OF ACTION (60% M.L.D. INTRA- VENOUSLY) |
|--|----------------------|---|
| | | |
| Pentothal | 1:17 | 28 |
| Evipal | 1:15 | 42 |
| Thio analg. of amytal | 1:15 | 45 |
| Alkyl secondary—butyl thiobarbituric acid | 1:8 | 97 |
| Nembutal | 1:6 | 130 |

M.L.D. = dosage of drug in mg. per kg. which kills 50 per cent of the animals (rabbits).

*In round numbers (Werner et al. [1937]).

in both cases, and one would expect that, if the very short-acting barbiturates are to be used orally, the variation between satisfactory intravenous and oral doses will be even greater than when the longer-acting agents are used.

Doses of various barbiturates used for production of similar periods of narcosis by oral administration must be inversely proportional to the duration of action obtained on intravenous use. This indicates that certain hazards will be introduced if any attempt is made to employ the very fast-acting barbiturates by any route which allows the situation to be complicated by the absorption factor, as it is in oral or rectal administration. The very fast-acting barbiturates are destroyed so rapidly in the body that, if they be used orally or rectally, the time required for absorption delays entry so that relatively large doses must be used. Individual variations in absorption rate render such practices dangerous. So it seems doubtful if the very fast-acting barbiturates can ever be used safely except by vein; at least, the slow routes of absorption are unpromising as long as the toxicity of these substances remains as high as it is. The very short-acting barbiturates when used by vein should, other things being equal, be safer for intravenous use than are the slower-acting ones. This is so because the very fast-acting agents are characterized by rapid induction, a rapid appearance of the maximum effect, and a rapid destruction. This permits a more precise control than is obtained with the slower-acting barbiturates.

It is interesting to observe that the ratio of the minimum lethal dose to the minimum hypnotic dose is similar for each of the five barbiturates studied here. The ratio is of the order of 5.

Anesthesia for Thoracic Surgery.—

Eversole and Overholt (1936) have pointed out that patients who must undergo thoracic surgery are often poor risks from the anesthetist's point of view. Suffering from protracted illness and long periods in bed, they may be in poor general condition. This group tolerates even slight

degrees of anoxia poorly. The absorptive surface of the lungs is reduced by the lesion. Abnormal quantities of mucus and pathologic secretions bathe the tracheobronchial tree. Coughing may be frequent. When the patient is placed upon the operating table, the good lung is down and its functioning volume is reduced by the weight of mediastinal organs and by a high diaphragm on the underside. It is cramped by the position of the patient and by supporting pillows.

It is generally agreed that local or regional anesthesia is satisfactory for drainage of empyema, thoracotomy for lung abscess, and for closed pneumolysis.

A detailed list of advantages and disadvantages of common agents is presented.

Beecher (1938) has considered the hazards to be overcome in determining the best choice of anesthetic agent and of anesthesia procedure in the difficult group of cases requiring surgery through the open chest. The chief hazards which the plan of anesthesia should be designed to overcome are: (1) obstructing secretions and blood in the airway; (2) troublesome reflexes, including cough; and (3) anoxia and circulatory strain.

Secretions or foreign material in the airway not only obstruct, but when sprayed over the good lung tissue may cause pneumonitis. Secretions and blood must be controlled, and they can be controlled through postural drainage before and during operation. The operation is carried out with the patient in the head-down position. Aspiration of the bronchi, as indicated throughout the operation, can also control secretions and blood. This necessitates the use of an intratracheal tube which should be inserted as soon as possible after induction of anesthesia. Cocainization of the pharynx is unnecessary for this procedure in most cases and adds to the hazards. The insertion of an intratracheal tube under local anesthesia (before general anesthesia is induced) may be justified if the sputum is very profuse. At certain periods during open chest operations, routine aspiration through the intratracheal tube should be carried out whether or not secretions can be heard in the airway. Notably, this should be done when the patient is turned on his side following induction and intubation, just after the pleura is opened, when the diseased lung tissue is mobilized, when the tourniquet about the lung stump is released, and at the end of operation before removal of the intratracheal tube. Finally, the liberal use of atropine in gr. $\frac{1}{100}$ to gr. $\frac{1}{75}$ doses given subcutaneously will help minimize the formation of troublesome secretions in the airway.

Troublesome Reflexes: Cough is normally initiated by local irritation in the air passages. The reflex can be set up by surgical irritation of the afferent vagal fibers in the pleura. Efficient cough requires a closed glottis and intact chest wall so that intrathoracic pressure may be built up. Efficient cough is impossible during open chest operations, not only

because of the impossibility of building up a relatively high positive pressure, but also because of the unfavorable position of the patient during this type of surgery. It has long been recognized that cough has a spreading action as well as expulsive action. When a person attempts to cough with an open chest, he produces a sudden herniation of the lung through the orifice; coincident with this there may be a spread throughout all parts of the lung of infectious or irritating material that may be in the airway. Since cough has a spreading action, it is of great importance to keep the airway free of infectious material. Cough during thoracic surgery dangerously increases the technical difficulties of the procedures undertaken. It is a mistake to preserve the cough reflex in this group of cases during operation. The anesthetist, not the patient, should assume the responsibility for maintaining free air passages.

Reflexes producing troublesome consequences are particularly likely to be set up by surgery at the hilum. Vagal stimulation occurs, leading to an irregular, jerky type of respiration interspersed with sudden periods of apnea, and the heart rate is slowed.

These troublesome reflexes can be minimized by the use of atropin, since this drug frees the vagus. At times it will be necessary to inject procaine directly into the vagus, as well as beneath the parietal pleura over an area about 15 cm. in diameter surrounding the pleura. Occasionally it will be necessary to eliminate the movements of the diaphragm on the side of the operation by injection of procaine directly into the phrenic nerve.

Anoxia and Circulatory Strain: The body's normal oxygen supply is hindered by obstruction of the airway and by the open pleura. The latter allows, as a result of the action of atmospheric pressure in the open chest and the respiratory movements, swinging of the mediastinum. Not only does this limit the aeration of the contralateral lung, but it gives rise to reflexes which probably are responsible for a fall in blood pressure. The open pleura interferes, then, not only with the intake of oxygen but with its distribution as well.

Several factors operate to reduce the circulating blood volume. In warm weather sweat loss is a factor. Pleural and mediastinal reflexes are important in the reduction of the volume of circulating blood. Also important are the circumstances which tend to produce shock, such as prolonged surgery and chilling. The heart is subject to great strain due both to direct pressure during the surgical manipulation and to anoxia. Generally this circulatory strain is latent and becomes apparent only if the patient is improperly handled at the end of the operation, as, for example, in careless, abrupt changes of position.

Anoxia produced as described above can be combatted in a number of ways. Atropin reduces the troublesome reflexes and diminishes the quantity of mucus and saliva formed. A closed anesthesia system and an intratracheal tube allow the administration of a constant high per-

degrees of anoxia poorly. The absorptive surface of the lungs is reduced by the lesion. Abnormal quantities of mucus and pathologic secretions bathe the tracheobronchial tree. Coughing may be frequent. When the patient is placed upon the operating table, the good lung is down and its functioning volume is reduced by the weight of mediastinal organs and by a high diaphragm on the underside. It is cramped by the position of the patient and by supporting pillows.

It is generally agreed that local or regional anesthesia is satisfactory for drainage of empyema, thoracotomy for lung abscess, and for closed pneumolysis.

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Two hundred and twenty-six patients (Coryllos and Bass [1939]) received avertin (average dose, 60 to 80 mg./kg.), with two deaths directly attributable to the avertin, according to the authors. Four deaths occurred the day of operation in this group.

The use of evipal anesthesia in 200 thoraeoplasties is described by Coryllos and Bass (1936). In these 200 cases the average initial systolic pressure was 123 mm. Hg, and the average minimal systolic pressure was 76 mm. Hg. In thirty patients the initial fall in blood pressure was so great that the systolic pressure could not be elicited at the arm. The authors refer to the "favorable results" of this type of anesthesia for thoraeoplasty, higher praise than most anesthetists would be willing to grant.

Gurd, Vineberg, and Bourne (1938, 1939) describe their experiences with the use of spinal anesthesia for thoraeoplasty. They have treated forty-two patients under spinal anesthesia. They have had two deaths in the operating room and three other bad seares, all of which are attributed to the anesthesia. It is surprising to find, notwithstanding this experience, that the general tone of the paper gives favorable consideration to this type of anesthesia for these cases. It is also surprising to find the statement that they have not noted phrenic root paralysis with interference with functioning of the diaphragm, surprising when the paper mentions two deaths and three bad seares. The only case described in detail is one typical of this latter group; respiratory and cardiac failure both occurred here. Also, "less bleeding" accounted for by a drop in blood pressure would scarcely seem to be an advantage. This paper hardly raises the reviewer's enthusiasm for spinal anesthesia for thoraeoplasty.

Newton (1935) has used spinal anesthesia in twenty-eight consecutive thoraeoplasty operations. He advises its use in selected cases, in patients "with mental poise." He states that in patients under spinal anesthesia he sees less shock than in patients under nitrous oxide, local and avertin. Possibly so, but neither of these choices seems desirable to this reviewer.

Lundy, Tuohy, Adams, and Mousel (1939) advocate the use of spinal anesthesia for lobectomy and total pneumonectomy because "the patient is able to cough and raise mucus." They also claim that its use reduces the danger of postoperative pneumonia or infection of the good lung with mucus from the affected side. The reviewer disagrees with this. An efficient expulsive type of cough is not possible with the chest wall open. A cough with the chest open, when the airway contains irritating, infectious material, is likely to spread the sputum and it increases the danger of postoperative pneumonitis.

Burnett (1937) describes the use of local anesthesia for a one-stage pneumonectomy.

A good deal has been written (cf. Burford [1938]) about sudden massive collapse of one or both lungs during anesthesia, followed by

centage of oxygen and the use of positive pressure anesthesia whenever it is needed to inflate collapsed portions of the lung, to restore or maintain a good blood color, or to aid in stabilizing the mediastinum. The head-down position promotes drainage; it perhaps minimizes the possibility of cerebral emboli, and it aids in maintaining an abundant blood supply to the vital centers. Intravenous fluids, blood in particular, sustain the circulating blood volume notwithstanding the tendency to a decrease in it during surgery in the open chest. Blood transfusion also counteracts the copious postoperative weeping of the pleura, with the consequent loss of, in many cases, 500 c.c. or more of blood plasma.

Choice of an Anesthetic Agent: The choice is considerably limited by the exacting requirements of this group of cases, as outlined above. Ether seems to fit the requirements best, because of the high oxygen percentage one can use with it, the tolerance of the circulatory system for it, the low toxicity of the agent, and, finally, its low mortality. The use of avertin for these cases is not desirable because of its depressant action on the respiration and circulation and its high mortality. Cyclopropane cannot be unreservedly accepted, chiefly because of its to date inadequately evaluated toxic cardiac effects. Spinal anesthesia, preferred by a few intrepid surgeons, violates all of the requirements outlined at the beginning of this paper and is not suitable for this group of cases.

Various Agents: Rovenstine (1936) describes the use of intra-bronchial tubes for open chest surgery.

Coryllos and Bass (1939) describe the use of several anesthetic agents in 1,370 cases undergoing thoracic surgery, chiefly thoracoplasties. Three hundred cyclopropane anesthetics were administered to this group. They report that "in many cases there was a marked drop in blood pressure with coincident shock as soon as the mask was removed at the end of operation." They believe that bleeding is increased under this agent over that of other agents. The most arresting information contained in their paper is the report that they encountered five cases of generalized convulsions and three others with localized muscular twitchings in 300 cyclopropane anesthetics for thoracic surgery. These led to death in three cases. In comparison with this, they refer to 1,600 previous thoracic cases, with only one convulsion. In the 300 cases under cyclopropane, ten died twenty-four hours or less after operation, one patient dying during induction.

Brown (1938) states that ether is contraindicated for use in pulmonary tuberculosis. His statement is based upon its use in ten operations for treatment of pulmonary tuberculosis. The reviewer takes strong exception to this statement, based upon a five-year experience at the Massachusetts General Hospital where several hundred thoracoplasties have been carried out under ether anesthesia, with exceptionally satisfactory results. This material is being prepared in detail for publication.

of tetanus in man. However, statistical analysis of the data presented indicates that the differences between the control and the anesthesia groups are not significant, except in one (out of four) cases in which the differences shown are possibly significant but not clearly so. More data might substantiate Firor's statements; those presented fail to do so.

Anesthesia in the Treatment of Tetanus.—

Chia (1938) has successfully treated a case of advanced tetanus with, among other things (wound surgically cleaned, antitoxin, hydrogen peroxide in the wound, etc.), avertin anesthesia (four rectal injections on four successive days, 80 mg. per kg. at first, then 60 mg./kg.). Potassium bromide and chloral were also used.

O'Farrell (1938) describes one patient with advanced tetanus who recovered following prolonged pentobarbital anesthesia (as well as specific treatment).

HAZARDS AND COMPLICATIONS OF ANESTHESIA

Reports of Postoperative Pulmonary Complications.—

If one were to judge from the many papers written on the subject, it would seem that a major occupation of anesthetists was the compilation of statistical studies regarding the incidence of postoperative pulmonary complications under various agents. The chief interest of such studies appears to be centered in demonstrating that the newest agent occasions the lowest number of postoperative pulmonary complications in comparison with the longer used agents. One's faith in the value of such studies is considerably weakened by finding that what purport to be statistical analyses have in all but a very few cases failed to take into account the most rudimentary requirements of statistical analysis. The casualness with which many writers undertake statistical analyses does not alter the fact that such matters are involved, time-consuming, and utterly valueless unless the fundamental laws of statistics are observed. Unhappily, statisticians and their statistics are looked upon with suspicion by the rest of the world. To be sure, statistical methods are not a substitute for common sense; on the other hand, some use of such methods is necessary if common sense is to be preserved in the handling of quantities of data.

Whenever this reviewer is confronted with a new series of data which tends to show that one anesthetic agent is followed by fewer postoperative pulmonary complications than another, several questions come to mind. If the anesthetic agent is of considerable importance in this regard, why is it that men are found to have many more of these complications than women? The ratio varies from study to study, but the incidence is usually stated as from two to four times greater in men than in women. Every one is agreed, it seems, that upper abdominal operations are followed by a very much higher incidence of postoperative pulmonary complication than are lower

death of the patient. Naturally, death is to be expected if both lungs remain collapsed. It is difficult for this reviewer to accept the often-made statement that the sudden massive collapse of one lung is to be followed by death. In several hundred open chest explorations at the Massachusetts General Hospital the sudden massive collapse of one lung has not resulted in harm, and this with the activity of the good lung hampered by being on the underside. No portion of lung which is to be saved is allowed to remain collapsed during operation for more than about fifteen minutes, for if this time is exceeded the collapsed portion may become seriously edematous. Edema has been observed to develop while such collapsed portions were watched.

The breathing of an abnormally high percentage of oxygen during anesthesia will lead to collapse of peripheral portions of lung in unventilated regions. During periods of hypoventilation the proportion of unventilated and probably collapsed regions may assume important proportions. Accordingly, it seems desirable to use a little positive pressure—not more than 8 or 10 cm. H_2O for two or three minutes every fifteen minutes—when using a high concentration of oxygen in the gases inspired. This, of course, will not overcome the collapse due to plugged bronchi. Bronchial aspiration or bronchoscopy may be required to overcome this if moving the patient or coughing is not adequate at the end of operation. Others have attacked the problem by adding inert gases, such as nitrogen or helium (*loc. cit.*). In unpublished experiments in dogs Beecher found that only a few breaths of room air were sufficient to eliminate the danger of pulmonary collapse when the respiration was checked at about the time the animals were breathing high oxygen mixtures.

Anesthesia for Diabetic Patients.—

Hale and Tovell (1938), in considering the choice of anesthetic agents and methods for diabetic patients, conclude on the basis of observations of 279 anesthetics in 244 patients that the common anesthetic agents may properly be used in diabetic patients, providing the diabetes is carefully controlled pre- and postoperatively, and providing long surgical procedures or large quantities of ether are avoided. It is very important to avoid anoxia.

Wileox and Tovell (1939) have more recently considered this subject.

Firor, Lamont, and Shumacker (1940), in a study of the cause of death in tetanus, observed in dogs with general tetanus that the injection of a usually safe dose of nembutal would kill the animal in a short time. They also observed that, when tetanus toxin was given intravenously, the administration of enough nembutal or avertin to stop convulsions shortened life. While such observations must obviously be transferred to man only with great caution, Firor's reports offer a real challenge to a heretofore accepted part of the therapy

that the type of postoperative pulmonary complications found after gastric surgery, for example, are very unusual in this group. Emphasis on duration of anesthesia may in the future be shown to be justified; at the present time emphasis on other factors would seem to be equally, or even more, important.

Convulsions and Brain Damage During Anesthesia.—

Convulsions: In the past dozen years or so, increasing reports of convulsions during anesthesia have been appearing in the literature. This certainly does not mean that the phenomenon was unknown before 1927, when the first reports were made, but it is one more example of the value of calling attention to a morbid process: once described, many reports appear. A telling commentary on the confused state of our knowledge of this occurrence is offered by a glance at the numerous and conflicting suggestions as to etiology (cf. Beecher, 1938). Nearly as many suggestions as to cause are offered as there are writers on the subject. Most of the papers are based upon speculation. Their value lies chiefly in their case reports, for, in viewing these reports as a whole, certain fairly constant features stand out. These offer a working description, as far as it goes, of the phenomena. A typical convulsion is described as usually starting with twitchings of the face. These quickly spread and soon involve the entire body in clonic convulsions which last from a few minutes to several hours. In the latter case they generally terminate in exhaustion, circulatory failure, and death. Children or young adults appear to be most often attacked. The case record often contains the statement that respiratory difficulties have preceded the onset of the process. Respiratory failure may occur during the convulsions.

Lundy (1937) has tabulated 144 cases, chiefly from the literature. It is evident that convulsions occur under several anesthetic agents. The term "ether convulsions" is misleading.

Brief references to a number of other recent convulsions during anesthesia follow. Chadwick (1936) refers to a case of "ether convulsions" successfully treated by intravenous evipal, as do Dodd (1937) and Taylor and Goldman (1938). Hunt mentions (1938) evipal in the control of convulsions from novocain. Shackleton (1937) reports two cases of convulsions during anesthesia, an ethyl chloride-ether sequence. Mennell (1937) reports "ether convulsions" occurring twice in the same patient. Human (1937) reports a convulsion during nitrous oxide-ether anesthesia. Cartwright (1937) discusses muscular twitches during anesthesia as a result of anoxia under nitrous oxide and other agents, and as a result of poor muscular relaxation with muscles under tension, and finally discusses "ether convulsions." He reports nine cases occurring under several agents. The temperatures rose to 109° F. Daly (1937) reports two "ether convulsions." Thierry (1938) has collected a number of anesthesia convulsion cases from

abdominal operations. If the anesthetic agent plays any considerable role, why is this so? The condition and sex of the patient, the duration and depth of the anesthesia, and the operation have all been shown to be important factors. Surprisingly often, observers have reported the same general incidence of complications following a given operation (with like conditions) under general, local, or spinal anesthesia. If the anesthetic agent itself is of much importance, these studies must be in error. Both points of view cannot be correct. Where the truth lies is uncertain. It will scarcely be revealed by the typical study of the matter to be found in the literature.

As far as pulmonary complications are concerned, comparison of postoperative results in one hospital with those in another is a hazardous and uncertain procedure of highly questionable value. Certain it is that none but the most remarkable difference needs cause any comment. Instructive comparisons are rare. In the case of postoperative pulmonary complications, the general experience has been that, when complications are looked for in succeeding years, the number found is directly proportional to the interest and duration of the study. Type of patients, housing conditions, and the abilities of the surgeon and anesthetist all vary, so that comparison of results is probably of little value.

Dr. Waters (1936) wisely summed up the matter when he said, "I think the teaching usefulness of records is to the man who keeps the records rather than to others in general."

It is sometimes stated that the duration of an operative procedure greatly influences the incidence of postoperative pulmonary complications, and yet there are many reasons for questioning the role of duration per se. However, prolongation of deep anesthesia, like other procedures which greatly tax the patient, is probably important in increasing the incidence. For example, few major respiratory complications occur following obstetric and gynecologic operations. Many gynecologic operations last a very long time. It seems nearly impossible to this reviewer to dissociate the factors which require the long operation, the blood loss incidental to it, the traumatic reflexes, the tissue damage which may accompany operation, the prolonged anesthesia, and often the long operations mean the surgeon was in trouble, and many other factors, all of which probably play a part in determining the average higher incidence of postoperative pulmonary complications following long operations. Duration of anesthesia itself may not be of so much importance as other specific factors which operate during the time recorded. Such data may give a false impression of the advantages to be gained by speed. The uniformly longest operations at the Massachusetts General Hospital are those that involve surgery in the open chest. After several hundred such operations (most carried out under ether anesthesia), it can be said

The damage to the brain in the four cases appeared to be due to nerve cell deprivation of oxygen.

Henson (1937) refers to a delayed depression which resulted in death following the use of cyclopropane for a herniorrhaphy.

Lowenberg and Zbinden (1938) report further cases of brain damage under nitrous oxide anesthesia. They continue to attribute the damage found to a specific toxicity of nitrous oxide rather than to accompanying anoxia, and their arguments for this continue to be unconvincing to this reviewer.

Considerable debate has occurred as to whether the brain damage sometimes found after nitrous oxide administration is in truth due to accompanying anoxia or to a specific toxicity of the anesthetic agent. Pertinent here is a brief comparison of the effects of nitrous oxide and a simple asphyxial gas like nitrogen (Courville, 1938): (1) Under nitrous oxide the pulse is more rapid (the cardioinhibitory mechanism is less effective); (2) convulsive movements are less apparent under nitrous oxide, perhaps as a result of depression of motor nerve cells; (3) respiration fails sooner under the anesthetic agent, due to a specific depressant action on the respiratory center. Nitrous oxide produces depressant effects which disappear when nitrogen is substituted for it. Unquestionably, nitrous oxide has a true anesthetic effect. It is well known that true nitrous oxide anesthesia can be produced in many cases only at the lower limit of adequate oxygen supply. That this limit is often exceeded is demonstrated by the frequency with which cyanosis appears before true anesthesia can be produced. The zone under consideration is a borderline one, and it is accordingly difficult to reach a reasonably certain conclusion as to whether specific action of the nitrous oxide or asphyxia is responsible for the accidents reported. The evidence appears, however, to incriminate the latter. Narcotics do not produce structural changes in nerve fibers or interstitial elements; on the other hand, any or all structures show morphologic change following asphyxia. The similarity of the lesions found (including nerve cell damage) following the accidents to those lesions known to be produced by asphyxia support the asphyxia hypothesis. When patchy necrosis is found in the brain, it is like that which appears following oxygen shortage. Such areas of necrosis have not been observed as a result of toxic action of narcotics without anoxia. Degeneration of the lenticular nucleus is commonly produced by asphyxia but not directly by narcotics. Such degeneration is common in these cases. It seems safest to conclude that the cerebral damage is the result of asphyxia rather than of a direct action of the anesthetic agent.

It must be recognized that the mechanisms producing oxygen shortage may vary widely. Lack of cyanosis does not necessarily mean the absence of asphyxia of fatal degree (cf. anemia, or localized anoxia

the literature and has presented one of her own. Dodd (1939) thinks atropin responsible for "ether convulsions," reporting four cases. Gitlin (1938) reports a convulsion in a patient under nitrous oxide-ether anesthesia. An "ether convulsion" treated with calcium is described by Steel (1939). He also administered in therapy of the convulsion 35 per cent CO_2 , later reduced to 17 per cent. There was recovery notwithstanding the high CO_2 inspired. Smith (1938) has attempted to show that a variety of complications during and after operation, including "late ether convulsions," may arise through derangement of the heat-regulating mechanism of the body, occasioned by overheating. He reports three cases of convulsions during anesthesia. Postconvulsive temperatures are given. Pinkerton (1938) reports one case of convulsions during anesthesia, an ethyl chloride-ether sequence. He reports postconvulsion rise in temperature, but the temperature had been elevated preoperatively.

Bradshaw (1939) reports a convulsion during anesthesia and includes data on ether kept and analyzed at weekly periods for a year. Tests for aldehyde, peroxide, and acid were made during this period. Only one sample showed a positive test (aldehyde), and that after ten months.

Griffith (1938) reports a convulsion during cyclopropane anesthesia. The convulsion appeared forty minutes after nasal packs soaked in nupercaine had been inserted and may have been due to this agent. The convulsion was controlled by intravenous sodium amytal.

One convulsion during cyclopropane anesthesia has occurred at the Massachusetts General Hospital. This was checked by intravenous sodium phenobarbital. (See also the case of Gebauer and Coleman [1938], referred to below.)

The extraordinary results of Coryllos and Bass (1939) are arresting. They encountered five cases of generalized convulsions and three others with localized muscular twitchings in 300 cyclopropane anesthetics for thoracic surgery. These convulsions were followed by death in three cases. In comparison with this, they refer to 1,600 previous thoracic cases under other anesthetics with only one convulsion.

Encephalopathy: Steegman (1939) reports four cases of encephalopathy following anesthesia, two after nitrous oxide, one after avertin, and one after cyclopropane, previously reported elsewhere. The cyclopropane case (Gebauer and Coleman [1938]) was that of a young woman who underwent a thoracoplasty for pulmonary tuberculosis. She was cyanotic following the operation, not during it. Convulsions appeared thirty-six hours postoperatively. She had a hyperthermia and at post mortem exhibited acute ulceration of the urinary bladder, acute hemorrhagic erosion of the gastric mucosa, and fatty infiltration of the myocardium. The brain was swollen.

subjects to the use of 6 or 9 per cent oxygen were such as to suggest that the prolonged use of more than from 85 to 88 per cent nitrous oxide is unwise.

In considering anesthesia for intracranial surgery, Brennan (1938) describes the rise in cerebrospinal fluid pressure in man (four patients) under avertin anesthesia. This may be due to accompanying respiratory obstruction, perhaps to anoxia. Intracranial pressure seriously increases under ether, he finds. The use of a wide intratracheal tube is a great aid in reducing intracranial venous congestion. Cerebral venous congestion under nitrous oxide-oxygen anesthesia is usually due to inadequate oxygen, respiratory obstruction, or faulty position.

Complications of Spinal Anesthesia.—

Circulatory and Respiratory Depression During Spinal Anesthesia: The cause of the fall in blood pressure and the cause of respiratory depression during spinal anesthesia have been studied intensively recently. It has been considered that the primary fall in blood pressure during spinal anesthesia depends upon peripheral vasomotor paralysis.* Strong evidence supporting this has been obtained by studies which show the absence of this fall in pressure in sympathectomized dogs and cats. For further information see Bacq, Bouha, and Heymans (1934), Wilson, Roome, and Grimson (1936), and Bradshaw (1936). Of course, the total fall in pressure is due not only to this mechanism.

Several other mechanisms have been suggested as accounting for the fall in pressure beyond the level caused by peripheral vasodilatation. Nowak and Downing (1938) group these as follows:

1. Central anoxia secondary to the peripheral vasodilatation.
2. Central anoxia resulting from intercostal nerve paralysis and from paralysis of the phrenic nerve roots.
3. Medullary paralysis following direct extension of the anesthetic agent.
4. Central vasomotor and respiratory paralysis as a result of vascular absorption of the drug.

In an effort to appraise the relative importance of indirect central effects due to primary peripheral changes as opposed to direct central effects, they have undertaken a study of blood gases. They find in cats under spinal anesthesia and light ether anesthesia that, whereas the arterial oxygen is little depressed, a considerable reduction occurs in the venous oxygen. They state that the increased arteriovenous oxygen difference is easily compensated for unless the phrenic or medullary centers are depressed or paralyzed. The validity of conclusions about spinal anesthesia drawn from this combination of ether and spinal anesthesia seems open to question. The well-known effects of ether upon the spleen and other blood reservoirs, its effect upon the heart muscle and respiration, etc., all seem to complicate the problem too much for definite conclusions to be reached.

*However, see the article by Smith, Roventine, and co-workers (1933).

as from localized ischemia, etc.). Asphyxia may be slowly and gradually accumulative, or it may be sudden through great obstruction of the airway, rapid cessation of respiration, or swift cardiac and circulatory impairment.

Abbott and Courville (1938) report a fatal case of severe degeneration of the globus pallidus following anesthesia. The authors conclude, on the basis of this case and the great majority of cases they have seen following carbon monoxide poisoning, that the globus pallidus of the lenticular nuclei is the region of the brain most sensitive to the effects of asphyxia. They believe the asphyxia which may have accompanied the anesthesia to be responsible.

It is unfortunate that this paper carries the implication in its title that nitrous oxide anesthesia was responsible for the accident, although on examination one learns that the patient received 6 grains of amytal (? by mouth), followed by nitrous oxide, ether, and ethylene. The paper contains the statement, "The damage to the brain was probably sustained during the period of cyanosis which began when ethylene was substituted for nitrous oxide." It had been stated earlier, that "cyanosis was thought to be due to spasm of the epiglottis." Granting that anoxia appears to be the likely cause of the disaster, certainly no evidence is presented that nitrous oxide ought to be incriminated over the other agents employed. While the reviewer has no wish to minimize the great hazard of anoxia during nitrous oxide anesthesia, the current tendency to attribute all neurologic accidents to asphyxia accompanying nitrous oxide anesthesia when this may be only one of several possible factors, is scarcely reasonable.

Fatal cerebral complications following nitrous oxide anesthesia in an obstetric patient are described by Brown, Collins, and Vaughan (1938). The oxygen percentage was, on occasion, allowed to get as low as 8.

Ford, Walsh, and Jarvis (1937) report the case of a young man who, following spinal, nitrous oxide and ether anesthesia with respiratory failure, presented grave brain damage. They suggest that anoxia alone may not be adequate to account for this damage, but that toxic action of the anesthetic agent plus asphyxia may be responsible. It seems unnecessary to postulate any cause other than anoxia in this case.

Much evidence is at hand to indicate that anoxia necessarily accompanies attempts to produce deep nitrous oxide anesthesia, if other depressant drugs have not been used. Bennett and SeEVERS (1937) have carried out experiments to find at what level anoxia contributes to the depressant action of nitrous oxide in normal men and whether or not anoxia produces a significant elevation of the sensory threshold for painful stimuli. They conclude that the oxygen intake must be reduced so low that the resulting anoxia is liable to contribute to post-operative morbidity (cf. Courville) before a significant increase in amnesia, analgesia, or anesthesia occurs. The responses of the normal

Donald and Watkins have investigated the matter experimentally and have produced with the agent a typical cauda equina syndrome (in cats): paralysis of the bladder, sphincter ani, and tail, sometimes weakness of the hind limbs, and also impairment of sensation.

Since the incidence in man is less than 1 per cent, for experimental purposes the dosage was stepped up to approximately five times that employed in man. Their experimental results (in cats) are shown in Table IX.

TABLE IX

| AGENT | TOTAL NUMBER INJECTED | NOT PARA- LYZED | PARALYSIS OF BLAD- DER, ANAL SPHINCTER AND TAIL | PARALY- SIS OF TAIL ONLY | TOTAL NUMBER PARALYZED | PER- CENTAGE PARALYZED |
|---|-----------------------------|-----------------------|---|-----------------------------------|------------------------------|------------------------------|
| Alcohol and glycerin | 23 | 23 | - | - | - | - |
| Heavy duracaine | 23 | 10 | 9 | 4 | 13 | 56 |
| Procaine 10 per cent (planocaine brand) | 10 | 5 | 2 | 3 | 5 | 50 |
| Procaine 10 per cent (novocaine brand) | 23 | 17 | 4 | 2 | 6 | 26 |
| Stovaine 5 per cent (Barker) | 10 | 4 | - | 6 | 6 | 60 |

These results appear to demonstrate that the toxic agent is the procaine itself. The above figures do not, of course, establish any difference between brands of procaine. The failure to produce a single case of paralysis following alcohol and glycerin seems to rule them out as the toxic agent and also disposes of the idea that the condition results from needle trauma.

Table X (MacDonald and Watkins, 1938) is of interest.

TABLE X

RELATION OF PROCAINE-HCl DOSAGE TO INCIDENCE OF SYMPTOMS

| PERCENTAGE CONCENTRATION | NUMBER OF ANIMALS | NUMBER SHOWING SOME PARALYSIS | PERCENTAGE PARALYSIS |
|-----------------------------|----------------------|----------------------------------|-------------------------|
| 2.5 | 20 | 0 | 0 |
| 5.0 | 20 | 2 | 10 |
| 10.0 | 56 | 24 | 43 |
| 20.0 | 8 | 4 | 80 |

This study, as the authors are aware, does not settle the matter of whether the addition of alcohol and glycerin enhances the toxic action of the procaine.

From this study it is plain that, in the concentrations ordinarily employed in man, commonly used spinal anesthetic agents are toxic to animals' nerve tissue to a serious degree. In man, however, their greater and more rapid dilution with cerebrospinal fluid prevents, except in rare cases, such paralysis. When such paralysis does occur,

Bonnycastle (1939) finds that the phrenic nerve roots in the spinal dural sac (of dogs) are paralyzed by concentrations of procaine which are less than those the respiratory center can withstand. He has found that the respiratory center can withstand concentrations of procaine somewhat greater than 1 per cent.

Shaw, Steele, and Lamb (1937) have studied the effect of spinal anesthesia upon the oxygen in the arterial and the venous blood (of dogs). They report an increase in the oxygen saturation of the arterial blood, a decrease in the oxygen content and saturation of the venous blood, and an increase in the arteriovenous oxygen difference; a stagnant type of anoxia was found to exist.

CoTui (1938) emphasizes the danger of using CO_2 as a respiratory stimulant when much of the sympathetic nervous system is paralyzed as it is in spinal anesthesia. Here CO_2 has a special "toxicity"; it lowers blood pressure by increasing peripheral capillary dilatation. However, Smith, Rovenstine, Goldring, Chasis, and Ranges (1939) report that "in human subjects with spinal anesthesia up to T3 or T2, and in whom all vasomotor reflexes other than those involving the head and arms are demonstrably blocked, neither CO_2 nor anoxemia has any depressor action" upon the circulation. This needs further checking.

CoTui points out that paralysis of the sympathetics checks adrenine secretion, and the loss of this may be responsible for some of the fall in blood pressure under spinal anesthesia.

Burstein (1939) recalls the work describing how a number of homeostatic mechanisms fail during high spinal anesthesia, in particular CoTui's emphasis upon the loss of compensating vasoconstriction when a considerable segment of the spinal cord has been paralyzed; Tournade and Schotte's demonstration of paralysis of the adrenalin-secreting mechanism; and paralysis of the sinoaortic mechanism as described by Heymans. Burstein calls attention to the fact that dogs are unable to compensate for postural blood pressure changes during spinal anesthesia as they can before and after. This is scarcely surprising, in the light of the above impairments.

Neurologic Damage Following Spinal Anesthesia: While persistent paralysis of nerve roots following spinal anesthesia is probably a rare event in well-established clinics, its occurrence is a serious complication of anesthesia. Ferguson and Watkins have investigated a series of cases in which paralysis (cauda equina syndrome) has followed the use of spinal anesthesia in man. They report that such damage is particularly liable to follow the use of duracaine. Duracaine heavy is said to have contained procaine HCl, planocaine brand, gliadin, and glycerin in a dilute solution (15 per cent) of ethyl alcohol. Later gum acacia was substituted for the gliadin. Since considerable uncertainty attached to which of the constituents was responsible for the toxic effects, Mac-

I. Errors of technique.

A. Inaccurate punctures.

B. Faulty postural arrangement of the patient.

II. Inactive solutions.

III. Cord tumor, rarely.

They report two cases in which three uneventful injections in each patient (pantocain used most often) failed to produce more than an extremely small effect. The above three chief sources of error seemed to be ruled out.

The phenomenon of sensitivity to the agents used in spinal anesthesia is well established. Perhaps true resistance also exists and should be classified as an idiosyncrasy. However, when the reviewer's "spinals" fail, he prefers to attribute the failure to shortcomings of his own technique.

Thompson (1934) reports a case in which spinal anesthesia for operation on a large tumor of the cauda equina was attempted. The injection of 100 mg. of procaine into the lumbar subarachnoid region, above the tumor, produced a girdle of anesthesia above the level of the tumor, yet complete sensation was retained in the operative field. These observations are of particular importance because they support the assumption that drugs used in spinal anesthesia produce their effect by a blockade of impulses in the spinal root filaments rather than by a direct action on sensory fibers in the cord itself.

Sensitivity or Idiosyncrasy to Anesthetic Agents.—

Gömöri (1936), in reviewing many accidents under local anesthesia, divides the accidents into two rather distinct groups. In the first group he places the cases which present a true intoxication resulting from overdosage. Here typical symptoms and signs are: psychic excitation, mental confusion, transient palsies, violent clonic convulsions. Fatalities are uncommon in this group. The second group is composed of those cases which show hypersensitivity to the drug used. Analysis of cases falling into the second group demonstrates that the quantity of the anesthetic used in the great majority of cases was extremely small; the concentration employed was well within safe limits; safe quantities of epinephrine were used. Outstanding symptoms and signs are anxiety, dizziness, paleness with or without cyanosis, a clammy, cold skin, extremely feeble pulse, and often loss of consciousness; often muscular twitchings, even convulsions, are observed. Death frequently occurs within a few minutes of the onset of symptoms.

Goodman (1939) discusses cutaneous hypersensitivity to the procaine anesthetics and correlates hypersensitivity with chemical structure. He also makes the interesting observation that persons whose skins manifest the very highest degree of contact-type allergic eczematous sensitivity do not necessarily exhibit sensitivity of their mucous membranes.

it is usually of greatly limited extent. In the experimental animal the bony canal is more completely filled with nervous tissue, and a relatively smaller amount of cerebrospinal fluid is available for diluting purposes.

Lnndy, Essex, and Kernohan (1933), following a prolonged temporary paralysis in man from the use of 10 per cent procaine, employ from 3 to 5 per cent solutions of procaine as they leave the syringe. There seems to be no excuse at this time for injecting greater than 5 per cent solutions of procaine into the subarachnoid space.

The work of MacDonald and Watkins emphasizes the value of a relatively slow spinal injection of anesthetic agents.

Ferguson and Watkins (1938) report fourteen cases of the cauda equina syndrome following spinal anesthesia. In thirteen of the cases heavy duracaine was used, and it probably was used in the remaining one. During this period some 1,700 spinal anesthetics were administered, most with duracaine.

References to damage from other agents used for spinal anesthesia are included.

Three of the cases came to autopsy. The sacral nerves showed fine vacuolation and were considered to show evidence of recent degeneration.

Kelman and Abbott (1938) have reviewed the literature on neural complications following spinocaine and other agents used in spinal anesthesia. They present five cases of prolonged neural damage following the use of spinocaine. Although the authors do not present desirable data regarding the total number of patients who received spinocaine, the fact that five cases of serious damage came under their observation is in itself a warning to caution in the use of the agent.

Koster, Kasman, and Shapiro (1937) attempted to produce in patients postspinal anesthesia headache, without success. A considerable bibliography is provided.

Foss and Bush (1939) present data on mortality and complications of spinal anesthesia.

"Rachiresistance": Schrechts (1934), in considering the variations encountered in the clinic to a given spinal anesthesia technique, attributes some of the unexpected results to variation of individual susceptibility to the drugs employed. When unusually profound anesthesia follows the use of a normal dose of an agent, he terms the patient "rachisensible." When the anesthesia is insufficient or non-existent, the patient is termed "rachiresistant." He believes this characteristic to be familial! He has found five members of one family to be "absolutely" resistant to spinal anesthesia (novocaine).

Black and Walters (1937) have reviewed the chief reasons for failure of spinal anesthesia:

curred recently is a strong indication that the explosion hazard from static electricity is greater with cyclopropane than it is with ether.

Horton (1939) has considered the factors which affect the occurrence and prevention of electrostatic sparks during anesthesia. He finds that a high relative humidity is not adequate to prevent the building up of large charges in an operating room. In itself it is an inadequate safeguard. He recommends that any electrical interconnection in close proximity to the breathing tubes, the mask, or other portion of the rebreathing system be discontinued. Cushioned stools should never be used in the operating room. Woolen blankets and wool or silk outer garments should be prohibited.

When closed anesthesia systems are used, it is probable that no explosive mixture will exist beyond the radius of a foot surrounding a leak. This, of course, does not apply if the anesthetic mixtures are deliberately discharged into the room.

Horton discusses the dangers of grounding patients. These arise in the danger of an electrical shock coming from the electrical equipment in use, as well as from the increased hazard of an electrostatic spark between the grounded system and a nongrounded person who, through error, might approach the system. He also points out the hazards of low resistance intercoupling of patient, operating table, gas machine, and anesthetist. He recommends the use of high resistance intercoupling. Such intercoupling requires conscious effort. If imperfectly arranged, it may lead to a dangerous sense of security.

An alternative to Horton's system might be for the anesthetist to maintain constant contact with the patient (away from the airways) and frequent contact with the other bodies (operating table, gas machine). If the contact must be broken, when the anesthetist resumes it, the patient should always be approached by making contact as far from the airways and any potential leaks as possible, always at least one foot from possible leaks. The reviewer is in no position to argue the merits of this system over that proposed by Professor Horton. It has some support in its considerable use. In any case, the anesthetist must take the responsibility for keeping all bystanders and members of the operating team at least one foot away from potential leaks.

Horton points out the hazards incident to the disconnecting of airways, breathing bag, etc., during operation.

Connell (1939) has considered the hazard of explosion from the point of view of the manufacturer of gas machines.

Five classes of ignition may produce explosions of combustible anesthetic mixtures:

1. Intermixing of combustible gases under high pressure.
2. Sparks due to mechanical friction.
3. Catalytic action. (This is of doubtful importance. Possible catalysts that need study are soda lime, dry metal oxides, the platinum

Hailey and Hailey (1937) report three cases of severe dermatitis following the use of nupercaine ointment.

Theodore (1938) reports a case of sensitiveness to larocain.

Kotz, Roth, and Ryon (1938) report the death of a patient (toxemia of pregnancy, toxic myocarditis) following 31 c.c. paraldehyde by rectum. They review the literature on paraldehyde.

See also the section on neurologic complications of spinal anesthesia.

Explosions during Anesthesia.—

Compared with other surgical risks, the risk of explosion of the anesthetic agent is statistically small. There are many intangible factors, however, which increase the importance of this above its numerical value. As with many newsworthy events, an explosion and the circumstances surrounding it may be greatly exaggerated, leading to bad relationships between the public and hospitals when such accidents occur. This is aside from the shock to all those intimately concerned. Woodbridge (1939) has considered the hazard of explosion from the point of view of the anesthetist. Answers to a questionnaire sent out by Woodbridge concerning explosion rate are as follows:

| AGENT | ADMINISTRATION | EXPLOSION RATE/100,000 |
|--------------|----------------|------------------------|
| Ether | 1,975,342 | 1.72 \pm 0.31 |
| Ethylene | 326,798 | 2.44 \pm 0.86 |
| Cyclopropane | 259,985 | 3.85 \pm 1.22 |

The standard deviations are so large that it is impossible to draw any conclusions as to difference from these data, as he is aware.

Woodbridge's data do not reveal whether the explosions were occasioned by the use of the cautery, the careless use of light, fires, electrical equipment, or by other easily preventable means, or by the dread static discharge. This, it seems to this reviewer, is one of the basic questions to be answered. If a surgeon decides that the use of the cautery in a questionable case is so important that he considers the risk of explosion justified and if a fatal explosion occurs, that is one thing. If, on the other hand, all precautions known have been taken and a static discharge sets off a fatal explosion, that is quite a different story. A very important question is: How often has static electricity caused an explosion of serious consequence and how often fatalities with the common anesthetic agents? While Woodbridge's data do not answer this question, the answer will perhaps emerge from the valuable data being collected by the American Society of Anesthetists.

The nearly universal opinion that ether, ethylene, or cyclopropane presents an equal explosion hazard must be challenged. It is probable that such a general belief grew out of the fact that each agent in its anesthesia range can develop an explosive force of fatal violence. Other factors must be considered, such as the violence of explosion, etc. The series of fatal explosions (static) under cyclopropane which have oc-

Among the usual hazards and precautions, Hasler (1938) points out the dangers from laryngoscope and bronchoscope if faulty insulation leads to spark (loose bulb, etc.). He also points out dangers of dry air effected by some air-conditioning apparatuses.

The (British) Medical Research Council is investigating the question of explosions from static sparks, with the assistance of the National Physical Laboratory. Their conclusions are to be published soon, it is stated.

The following writers have also considered the explosion hazard during anesthesia, but not so thoroughly as have Woodbridge, Horton, and Connell: Phillips (1936), Toland and Kroger (1937), Becker (1937), Thalheimer (1938), Kaye (1938), and Becker and Woltersdorf (1938).

Impurities in Ether.—

To what extent the complications of anesthesia are related to impurities in the ether used is not clear. We have little information as to how such impurities affect the conduct of anesthesia. A finding of Knoefel and Murrell in mice (1935) concerns the rate of production of anesthesia by ether containing aldehyde and peroxide. They report that, when small amounts of these agents are present in the ether, a significant slowing of the rate of induction occurs (measured by loss of posture). A likely explanation offered for this effect of the impurities is that they act by slowing the rate of entrance of ether into the blood stream.

They also report that 0.2 per cent aldehyde and 0.07 per cent peroxide do not significantly alter the acute toxicity of the "ether."

Ether From Large or Small Containers?—

The question of whether ether supplied in 27- or 55-pound drums is as satisfactory for anesthesia as that provided in from one-quarter- to one-pound cans is a matter of considerable economic importance. Hediger and Gold (1935) attempt to show that ether supplied in large containers is as satisfactory as that in the small ones, even though the ether from the large containers had been exposed to the air for as long as sixty-eight days.

This matter can hardly be considered settled as yet, for there is some evidence that one lot of ether will decompose faster than another one. To rule out this hazard, the study would have to consider many more drums than was the case here. Doubtless, frequent and thorough cleaning of the small containers filled from larger ones could eliminate the possibility of decomposition products gradually appearing in them, but such would always be a possibility unless this was taken carefully into consideration. The fire and explosion hazard of the nearly empty but vapor-filled large drums, as well as the general fire hazard of a large bulk of ether, cannot be disregarded. The problem is an involved one; it needs further study.

(To be continued. The references will accompany the last part.)

of mouth dentures; possible impurities in the agents used might be added.)

4. Ignition by open flame, sparking electrical apparatus and cautery, diathermy, high frequency apparatus, and x-ray apparatus. (These latter should never be used in the presence of inflammable anesthetic agents.)

5. Electrostatic spark. No degree of room humidity, however high, totally prevents the development of momentary static charges.

Safeguards from static electricity are:

1. Wet breathing circuit at start.
2. Condensation of patient's breath.
3. Use of an electrolyte solution (calcium chloride) to keep the rubber of the breathing tubes conductive. (Wipe new rubber over with 4 per cent calcium chloride and rinse the rubber each time it is washed with rinse water containing a few tablespoonfuls of this solution. This will tarnish metal.)

4. Intercoupling with high resistance safeguard.

5. Room humidification.

Anesthetic apparatus.

1. The apparatus should be constructed so that intermixture of gases at high pressure is impossible.

2. It should be constructed of sparkless metals.

3. It should be tight and with central spill valve.

4. The apparatus should not be subjected to open flame or electrical apparatus.

5. The apparatus should be emptied and washed free of combustible material when not in use.

6. Conduit connections, metal to metal, should not be disturbed or reconnected during use.

7. The apparatus should not be covered while idle.

8. Dry, hot blankets should not be carried past it when in use.

9. It should be intercoupled electrically with patient and anesthetist before anesthesia is started and this intercoupling maintained until after washed out.

10. Intercoupling should be remote from gas spillage and of the high resistance type.

11. Rubber parts should be treated with electrolyte and kept moist inside during use.

Eversole, Sise, and Woodbridge (1937) state that high frequency electrical apparatus should not be used in operating rooms in which cyclopropane is being used, because of the danger of sparking from scattered points in the vicinity of such apparatus. This includes x-ray apparatus as well as electrosurgical units for cutting and coagulation. They do not consider that the low voltage actual cautery presents this same sparking danger, although, of course, the glowing cautery itself could initiate an explosion.

Book Reviews

A Bibliography of the Writings of Harvey Cushing. By The Harvey Cushing Society. Cloth. Pp. 108, with frontispiece. Springfield, Ill. Charles C. Thomas, Publisher, 1939. \$5.

On the occasion of his seventieth birthday, the Harvey Cushing Neurological Society presented the late Harvey Cushing with a small tome containing a complete list of his papers and books by title, his vita, and a list of papers published by his associates from his clinics at Baltimore and Boston. Appended also are the names of those who successively were his assistants in neurological surgery and appointees in the surgical research laboratories at Baltimore and Boston.

During a busy life, Harvey Cushing wrote 13 monographs and more than 300 papers. An additional 327 papers written by his associates under his direction are listed too.

An annotation, acquainting the reader with the circumstances under which the books and papers were written and the occasion of their presentation, accompanies the title of each book and a large number of the papers. It is extraordinarily interesting to peruse these titles and to appreciate that they were the work of one man. *The Pituitary Body* (1912), *Life of Sir William Osler* (1925), *Consecratio Medici* (1928), *Intracranial Tumours* (1932), and *Meningiomas* (1938) are monographs, each of which represents the best effort of its kind. His papers on typhoidal cholecystitis and cholelithiasis (1898) and the experimental formation of gall stones (1899), the bacteriology of the upper portion of the alimentary canal written with L. E. Livingood, experimental studies on brain compression done in Kronecker's laboratory in Bern (1902), routine determination of arterial tension in operating room and clinic (1903), and his methods of accomplishing decompression in inoperable brain tumor (1905) are some of his early papers which foreshadowed his genius.

The number of persons among his assistants who have established themselves as leaders in their fields gives further evidence of the great genius of Harvey Cushing. He attracted the best talent and left an indelible stamp on all of them.

This monograph outlines the versatile and remarkable accomplishment of one man during a long life of unceasing labor. It is a most animating and exceptional record. The book can be recommended, not alone as a key to Harvey Cushing's papers, but also because it details the literary contributions of a singularly stimulating and useful life.

Harvey Cushing's Seventieth Birthday Party, April 8, 1939: Speeches, Letters and Tributes. Cloth. Pp. 146, with 9 illustrations. Springfield, 1939, Charles C. Thomas, Publisher. \$3.

The Harvey Cushing Society, during their eighth annual meeting held at New Haven, Conn., celebrated Harvey Cushing's seventieth birthday, April 8, 1939. The occasion was signalized by a dinner at which were read telegrams and greetings from admiring friends, pupils and former patients from all over the world. Arnold C. Klebs, of Switzerland, life-long friend of Cushing, returned for the occasion.

Review of Recent Meetings

THE SOCIETY OF UNIVERSITY SURGEONS

ALEXANDER BRUNSCHWIG, M.D., CHICAGO, ILL.

THE second annual meeting of the Society of University Surgeons was held Feb. 9 and 10, 1940, in New York City at the New York Hospital. Most of the papers presented at this meeting are to be found in this issue of SURGERY. Brief abstracts of other papers presented at that meeting are summarized herewith.

William J. German and Max Tefel, Yale University, Surgical Production of Collateral Intracranial Circulation. An Experimental Study.—The authors described a method of temporal and suboccipital muscle grafts to the surface of the brain in order to produce an accessory arterial blood supply. The animals employed were monkeys with experimentally ligated carotid and vertebral arteries in various combinations.

D. Henry Poer, Emory University, Atlanta, Ga., Clinical Experience With the Use of Di-Hydro-Tachysterol (AT-10-), in the Treatment of Ten Cases of Hypoparathyroidism.—The author in a series of ten cases of parathyroid tetany following thyroidectomy employed di-hydro-tachysterol and vitamin D₂. These were thought to be equally effective in controlling the symptoms and maintaining serum calcium levels near normal. Each preparation has advantages over parathyroid hormone if its use is continued over a long period of time.

Cobb Pileher, Vanderbilt University, Experimental Cerebral Trauma. II. Further Observations on the Fluid Content of the Brain Following Trauma to the Head.—Experiments by the author were presented and interpreted to show a marked stability of the fluid content of the brain tissue even after trauma. The author furthermore was of the opinion that his experiments suggested that cerebral edema would not occur in animals following trauma.

Thomas E. Wyatt and Cobb Pileher, Vanderbilt University, Experimental Cerebral Trauma. III. The Effects of Acute Uremia, of Venous Obstruction, of Hyperthermia, and of Intensive Irradiation on the Fluid Content of the Dog's Brain.—These authors studied the fluid content of various portions of the brains in dogs after bilateral nephrectomy, bilateral ureteral ligation, venous obstruction, severe hyperthermia and intensive irradiation. The percentage of fluid was slightly but consistently elevated in cerebral and cerebellar gray matter and in the brain stem after hyperthermia. The fluid contents of the brains in all other experiments were within normal limits.

Alexander Brunschwig, University of Chicago, The Localization of Evans Blue in Malignant Tumors.—The author reported selective localization of Evans blue in twenty of thirty patients with various types of malignant neoplasms following intravenous injections of 50 to 100 mg. of the dye.

and that stillbirths and death certificates on them are not correctly reported, probably largely as a result of insufficient data and inadequate examination.

The way is pointed to the most precise method of determination of the causes of natal and neonatal deaths and only with a regime such as the one employed by the authors will the cause of death in individual or large series of fetuses and infants be correctly determined. The difficulty encountered in comparing reported series shows the need of greater uniformity in terminology of just what constitutes abortion, prematurity, stillbirths, etc., and shows the difficulties arising in the absence of a uniform classification of causes of fetal and neonatal death.

The embryologic and anatomic descriptions of fetuses and their individual organs are not extensive, but yet they are adequate for a thorough understanding of the general and special pathologic problems that are encountered in death of these individuals. The pathologic findings and possibilities are described in detail.

The 1939 Yearbook of General Surgery. Edited by Evarts A. Graham, M.D. Cloth. Pp. 796, with 304 illustrations. Chicago, 1939, The Yearbook Publishers. \$3.

Perusal of this volume will give the reader a bird's-eye view of some of the more important contributions to the literature of surgery during the latter months of 1938 and the early months of 1939. One of the most valuable parts of the volume are the many editorial comments of the editor. He who becomes familiar with the *Yearbook of General Surgery*, by study, year after year, cannot help but absorb something of the conservative philosophy of the well-known editor. Where else can one find the reactions of one surgeon who speaks with authority on so many surgical problems. That the editor know his yearbook is apparent when one notes how often he refers to previous reviews in earlier years.

New and important papers on anesthesia, sepsis, and surgical technique are reviewed. The materials in the section on the biliary tract are particularly good. In this section and in the chapters on thoracic surgery, the reader is especially glad to have the editor's comments.

In an appropriate foreword Dr. Graham refers to those developments in surgery during the year which are worthy of particular notice. This book can be recommended enthusiastically to all general surgeons as affording a synopsis of some of the more important and practical surgical papers of the year that has passed.

Les "pièges" de la chirurgie en diagnostic et thérapeutique: Erreurs et fautes ou faits présumés tels conditions et limites de la responsabilité. By Prof. E. Forgue, membre de l'Académie de chirurgie, and Prof. Aimes, Professeur agrégé à la Faculté de Montpellier. Cloth. Pp. 509. Paris, 1939, Masson et Cie. 120 francs.

The intriguing title of this book, "Snares in Surgery," was selected by the authors in preference to "Errors and Faults in Surgery" because the latter might create the wrong impression. Fully cognizant of somewhat similar previous expositions, such as the German edition of Stich and Makkas, they have attempted, in a different manner, to present a collection of facts representing misfortunate occurrences more often than surgical errors and to define the legal responsibilities of the surgeon.

Dr. Cushing responded in a light vein to the numerous toasts and felicitations but concluded on a serious note, exhorting neurosurgeons to serious thought as well as action. Said Dr. Cushing: "Neurology, broadly speaking, is a field for thinkers as well as doers, and it is gratifying that the surgical doers for almost the first time in the history of medicine have come to be recognized as deserving of memberships in the societies of those otherwise engaged. This being so, we must look to it that we justify this recognition by the character of our work."

An appreciation of "Harvey Cushing at Seventy," written by Henry R. Viets and reprinted from the *New England Medical Journal*, contains a commendable appraisal of Cushing's surgical and literary activities. A reprint of a similar article by John F. Fulton, under the title of "Harvey Cushing and Roentgenology," relates Cushing's great interest in the technique of taking x-ray films during the early days at the Johns Hopkins University. The concluding paper of the monograph, entitled "Notes on the Formative Period of a Neurological Surgeon," written also by Henry R. Viets, relates some very interesting episodes from Cushing's life: of his interest in anesthesia, his unrivalled capacity as a note-taker on clinical cases, manifested as early as his internship at the Massachusetts General Hospital, the notes being adorned by artistic sketches, and finally of Cushing's role in initiating in this country clinical studies in blood pressure.

These fragmentary accounts of a versatile and great man will some day be recounted in appropriate biographies, for a life so distinguished has many lessons to teach.

Fetal and Neonatal Death. A Survey of the Incidence, Etiology, and Anatomic Manifestations of the Conditions Producing Death of the Fetus in Utero and the Infant in the Early Days of Life. By Edith L. Potter, M.D., and Fred L. Adair, M.D. Cloth. Pp. 207, with 31 illustrations. Chicago, 1940, University of Chicago Press. \$1.50.

This unique book brings together and correlates statistical, clinical, anatomic, and pathologic data on fetal and neonatal deaths in such a manner that one interested in any of its phases can quickly find a ready answer to his query. For the specialist caring to go into greater detail, an adequate bibliography is furnished at the end of each chapter. Heretofore, this information has not been readily accessible in any single text and the interested student or graduate would have been forced to consult innumerable articles and texts.

The book begins with statistical expressions which are in general use today and these figures prove, though the authors have not emphasized this specifically, that current methods of examination and reporting stillbirths and neonatal deaths are grossly deficient. For instance, a report of the stillbirths in the registration area of the United States indicates that 78 per cent of those delivered under four months are males. This gives a sex ratio of 355 males to every 100 females, a figure which is more than twice as great as the highest scientific estimate for the conception ratio and more than three times as great as the usually quoted sex ratio of term and near-term fetuses. This emphasizes the difficulty in determining the sex of the early fetus by casual observation of the external genitals and re-emphasizes the importance of careful external and internal examination by someone especially versed in such detection. Furthermore, the fact that only 26 per cent of 125 infants were proved by autopsy to have died of prematurity, whereas 57 per cent of a comparable series of 166 infants without autopsy were said to have succumbed from prematurity, indicates that the causes of death in this group of patients are not being accurately determined

WILLIAM J. MAYO
AND
CHARLES H. MAYO

In Informal Operating Garb

The book is divided into three parts. The first, which is the shortest, consisting of approximately 60 pages, is devoted to errors in diagnosis, indications for operation, prognosis, and technique. The cause of such errors and the means of their avoidance are indicated. The second part, consisting of about 108 pages, is concerned with the surgeon's legal responsibilities as regards indications and authorization of operation, anesthesia, overlooked foreign bodies, esthetic surgical procedures, burns and accidents due to therapy. The third and most extensive part deals with various surgical affections of the special regions of the body. The diagnostic and prognostic factors as well as therapeutic applications are discussed.

In the reviewer's opinion the most significant part of the book is that which is concerned with the definition of the legal responsibilities of the surgeon. More recently this subject has been gaining greater importance and its significance has not been sufficiently appreciated by the busy surgeon. The remainder of the book, which is concerned primarily with the recognition of one's errors and of their avoidance, is a valuable consideration. Moreover, the method which the authors have employed in their presentation is instructive and desirable. Whereas numerous references are made in the text, an appended bibliography obviously would have increased the reference value of this book.

Atlas of Surgical Operations. By Elliott C. Cutler, M.D., and Robert Zollinger, M.D. Cloth. Pp. 67, with 181 illustrations. New York, N. Y., 1939, The Macmillan Company. \$8.

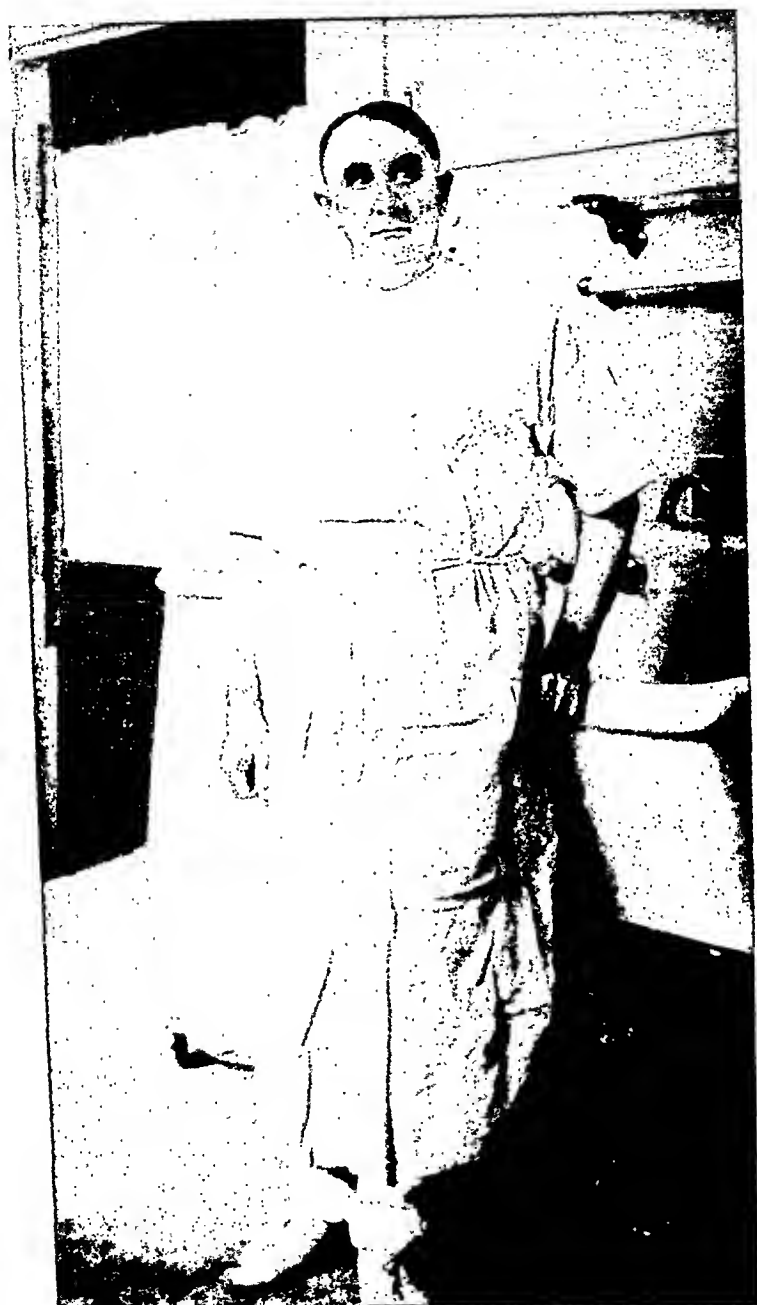
The authors' object in writing this book is to place in the hands of graduate students of surgery and surgical house officers a source book in which they may find described the intimate technical steps of surgical procedures. This objective the authors have accomplished, in the main.

Urological and neurological operative procedures unfortunately are not described; neither are thoracoplasty and operations upon the lung, esophagus, heart, or blood vessels, all of which the graduate student of surgery reasonably might expect to be found in an atlas of surgical operations. Failure to describe the closed or aseptic methods of intestinal anastomosis would appear to be a serious omission. Operations upon the pancreas are not described. Another defect is the omission of references.

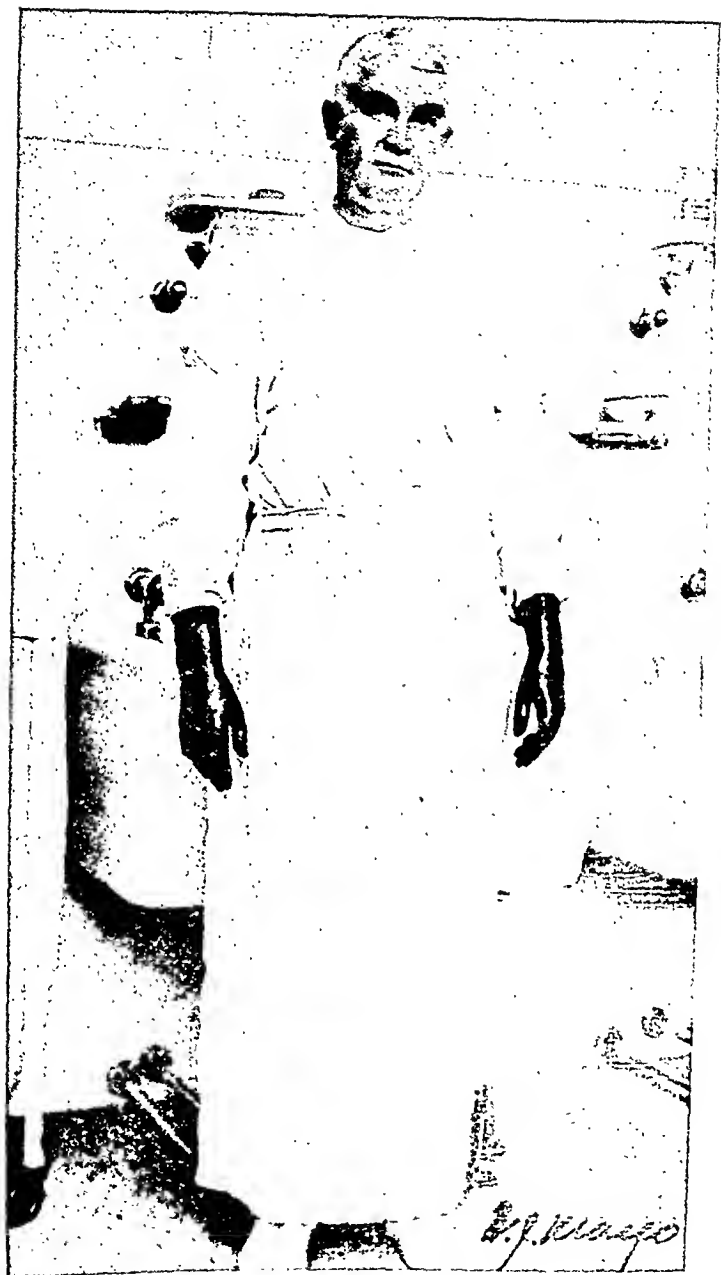
The illustrations are excellent, the descriptions brief and to the point. A studied effort has been made to preserve an effective and sequential relationship between descriptions in the text and the illustrations. The senior author's position among surgeons and his well-known interest in surgical technique promises a book reflecting the best precepts in the art and science of surgery. This expectation this compendium on operative procedure fulfills in an eminently practical manner.

Names are attached to operative procedures in the instance of hernia alone, in which section the names of Bassini, Halsted, Ferguson and Gallie are mentioned. The exteriorization operation upon the colon is described as the Mikulicz procedure; whereas, the Bloch or Bloch-Mikulicz would be a more proper designation.

This monograph may be recommended as a practical handbook on some of the commonly performed operative procedures practiced by the general surgeon.



CHARLES H. MAYO
1865-1939



WILLIAM J. MAYO
1861-1939

SURGERY

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Mayo Memorial Volume

A miscellany of papers written in honor of two
distinguished American surgeons

EDITORIAL PREFATORY NOTE

THE name, Mayo, has been engraved indelibly in the annals of surgery by the achievements of the brothers, William James and Charles Horace Mayo. Their own accomplishments and what they did for surgery will keep the name of Mayo unfaded in the memory of men when these printed words have grown dim with the desolation of time.

During their lifetime, the brothers Mayo declined modestly the suggestion of a memorial volume, acknowledging with a genuine expression of gratitude, however, this mark of esteem and affection of their friends.

These pages are written by admiring colleagues to do honor in death to the memory of two illustrious surgeons and distinguished Americans who lightened the burdens and brightened the lives of thousands of families. The influence of the work of these men has been felt wherever medicine is practiced, whether in the largest cities or the most remote places throughout the world. Their lives should be helpful and stimulating examples for surgeons everywhere.

home, the only notable exception being a visit which they made together to England in July, 1929, to be present at the dedication of a window they had given to the little parish church at Eccles, near Manchester, which their father had attended as a boy. In each clinical journey they had a specific purpose of learning some new surgical procedure by actual observation of its performance and of becoming acquainted with the leading surgeons of the world and their approach to the rapidly developing field of surgery.

From the beginning of their careers to the end, the brothers carried out in Saint Mary's Hospital both the application of the knowledge acquired in their travels and the contributions which they themselves made to surgical progress. At its opening, in 1889, Saint Mary's had twenty-five beds. From its beginning, this hospital received all classes of patients without regard to creed, color, or financial or social condition. A small band of the Sisters of Saint Francis was the administrative and nursing staff, and with few and untrained helpers these devoted women carried on the work. The confidence of the Sisters in Dr. William Worrall Mayo, for it was he who had supported them in the building of the hospital, was extended to the sons, and a perfect mutual understanding and trust continued throughout their lives.

This original group of physicians and nursing staff never lost the simplicity of method which was characteristic of the surgery of that time. In their surgical work the Drs. Mayo had the aid of Sister Mary Joseph, who died in the same year as the two brothers and of whom Dr. William J. Mayo wrote:

"In this early group Sister Mary Joseph, by reason of character, energy, and intellectual ability, took a prominent place. She became matron and director of the hospital, which position she held until her death. Executives of the caliber of Sister Mary Joseph are born, not made.

"Sister Joseph promptly mastered, to an extraordinary degree, surgical technique and procedures from the standpoint of the surgical assistant, a position in which she served for twenty-five years, working directly across the operating table from me. Possessing great keenness of perception, unusual clinical acumen, and an extremely delicate sense of touch, she aided me during the operations, performing technical maneuvers with rare facility. Her surgical judgment as to the condition of the patient, before, during, and after operations was equal to that of any medical man of whom I have knowledge. Of all the splendid surgical assistants I have had, she easily ranked first."

The unique relationship which existed between the Drs. Mayo and such a surgical assistant, who also was matron in the hospital, contributed in no small measure to the results of operations which the Drs. Mayo were able to report in their early years of surgical practice.

WILLIAM JAMES MAYO (1861-1939) AND
CHARLES HORACE MAYO (1865-1939)

DONALD C. BALFOUR, M.D., ROCHESTER, MINN.

IT WAS during the remarkable half century in the history of medicine from 1880 to 1930 that Dr. William J. Mayo and Dr. Charles H. Mayo lived their active professional careers, for they began the practice of medicine with their father, Dr. William Worrall Mayo, in the 1880's and continued their practice until their deaths in 1939.

In 1855 the father settled in southern Minnesota and began the varied practice of a pioneer physician and surgeon. His two sons in their early youth, while still in public school, often accompanied their father on his professional rounds and assisted him in those emergencies which largely comprised a general practice of that day, and in their summer vacations they gained a practical knowledge of pharmacy by working in a drugstore. There never was uncertainty as to their studying medicine. In later years Dr. W. J. Mayo wrote: "To grow up in a doctor's family with a professional background of some generations will likely have, as it did with my brother and myself, that sort of influence which leads, not to conscious choice of medicine as a career, but rather to unconscious elimination of every other choice. Neither my brother nor I ever had an idea of being anything but a doctor."

The incentive which led both brothers to train themselves for a surgical career may be found in their early experiences and in their father's interest in surgery, for in 1871 William Worrall Mayo reported the successful performance of an ovariectomy, and in the next thirteen years he carried out thirty-six similar procedures. There is also to be remembered the fact that William J. Mayo and Charles H. Mayo entered practice at about the period when the great advances of modern surgery were initiated.

The problem of acquiring a knowledge of surgery and keeping abreast of its advances was a difficult one to solve for these busy country practitioners in a small town. One essential in its solution was travel, and they were indefatigable, thorough, and persistent in this means of education. They early agreed that 25 per cent of their gross income from their practice should be set aside for education and research, and since their environment could not afford them adequate opportunities, they traveled in this country and abroad to observe the work of those who were more fortunately situated in regard to facilities, training, and clinical material. Their travels were on an exactly ordered plan, for they sought and saw only things that were done better than they could do them. One of the brothers always was at

was away, the other saw personally the patients on the services of both. Day by day, year after year, they observed an unvarying operating room ritual. For many years the brothers both operated every day, and their routine was much the same; that is, they began hospital rounds shortly after seven o'clock in the morning and operations promptly at eight o'clock.

As surgeons, William J. Mayo and Charles H. Mayo were distinguished by an amazing ability to focus on essentials and by good judgment based on enormous clinical experience. They were excellent technicians, carefully but not unnecessarily attentive to detail. While the two men differed in approach and technique, the work of each was marked by confidence, a high sense of responsibility, quick and steadfast decision and directness of attack. They were scrupulous in avoiding operation unless they believed the patient would be greatly helped, but they always offered the patient the benefit of operation if any doubt existed, particularly in the presence of malignant disease.

In all their years of intense activity in surgical practice they found time for daily reading and clinics. Dr. William J. Mayo for many years followed a routine of lying down between operations, and in these periods of physical relaxation he did much of his medical reading. He urged systematic medical study for surgeons and said: "I began by charging myself with one hour's study a day, and I did not give myself credit for advance work; that is, if I put in three hours, I took credit for one. I was scrupulous, however, in making up the deficit when it happened that I was unable to study. It is surprising how much one can accomplish by adherence to this type of program. The reading should be catholic. To the young surgeon I would say, do not read all surgery and technique, for technique is constantly changing. We abandon procedures which were perfectly satisfactory, for something which is no more satisfactory, as the ladies do their bonnets. Along with surgical literature, read medical articles in high class medical journals. Do not skim, but here and there select certain articles and read them with care, especially those that have a physiological background.

"Further, I would advise the young surgeon to write papers, and in writing to bear in mind what the old minister said, 'Few souls are saved after the first fifteen minutes of the sermon.' Write the paper not to show how learned you are, or to show the high type man who may be in the audience, that you are in his class. Rather, try to tell those in your audience, who perhaps may not know as much about the subject as you do, something that may interest and help them. Do not try to make too many points. . . ."

Throughout their careers these men carried on with their colleagues, a weekly conference for review of their own work and that of the profession in all parts of the world as represented in the literature and

Throughout the following years, the surgical work of the Drs. Mayo continued, and the results of their experience are recorded in the variety and character of their publications. Their writings stand as evidence of their numerous original contributions in many fields and of their recognition of the contributions of other surgeons and scientists. Their publications also are proof of their realization that to bring about advance in any field of surgery intense specialization based on adequate experience and knowledge of general surgery is necessary. In their early practice William J. Mayo and Charles H. Mayo were required to engage in every department of surgery, and it was only when they secured associates who were especially trained in many of these branches that they found it possible to restrict their own work to the surgical fields with which their names will always be associated.

The influence which these two men had on surgery and surgeons, on their associates, and on those whom they trained, came from the consistency with which they searched for the truth. From their earliest days of practice, the brothers, taught by their father, realized that the chief cause of error in diagnosis is incomplete examination, and in teaching and practice they stressed every means of acquiring as complete knowledge as possible of every patient. The early clinical records of both father and sons are models of careful observation and direct deduction. Their determination to know the truth led them to secure necropsies whenever possible and, as a result of their teaching, the division of pathologic anatomy in the institution they founded at present is granted permission for necropsies in over 80 per cent of deaths.

William J. Mayo emphasized always the desirability of utmost use of the physician's native intelligence in dispelling what he called "diagnostic fog"; by this he meant the confusing of the issue by too great reliance on laboratory and mechanical aids to diagnosis, invaluable though they are. In his homely and classic article, "In My Father's Time," he began by writing: "Clinical diagnosis in my father's time was based to a large extent on examination by the five senses aided by a few instruments of precision." The fact that the brothers were not eager to adopt the many new accessories which rapidly were offered for use in medicine and surgery may have had much to do with the development of their resourcefulness, their extraordinary clinical judgment and skill in diagnosis, and their adaptability to every sort of surgical situation. And throughout the years, in the building and development of their great adventure in group practice and medical education, while William J. Mayo and his brother and their associates encouraged every advance in medical research and employed every scientific aid, their sound common sense and wise discrimination were always evident.

In the early days the routine work of the office practice and the hospital required the personal care of the father and his two sons, and their unremitting feeling of mutual responsibility became a habit which carried through their entire lives. Always, when one of the brothers

sire to teach, with tolerance, patience, and consideration, with careful guidance, for the advancement and spread of knowledge, toward the better care of the sick and the strengthening of the profession. Their experiment in graduate medical education has established the soundness of the principles upon which they based their work and their teaching, for their methods have been continued on a university basis without radical change.

To have practiced medicine with distinction for fifty years and more, and to have won the respect and affection of colleagues and confreres, is a high achievement. William James Mayo and Charles Horace Mayo did not seek honors and rewards. The distinguished recognition which came to them they accepted with gratitude, untouched by pride and self-esteem, because they believed that it was bestowed not on them alone but also on those who had served with them in the work they loved.

by the travels of themselves and other members of the staff. I well recall that more than thirty years ago these meetings were held in alternate weeks in their two homes, and I remember the impression made on younger associates of the purpose of such conferences, to know the truth regardless of how unpleasant it might be.

Tolerant and understanding in all relationships, these brothers were exponents of freedom of speech and thought for their associates and themselves. In no way did they ever seek to interfere with religious, political, or social opinions, and they made this attitude a tenet of belief for the institution as a whole.

The Drs. Mayo were conscientious and enthusiastic in their attendance at the meetings of medical societies: county, state, district and national, special, and international. They believed and taught that a physician's standing in the medical profession depends on the manner in which he realizes his duty to medical organizations; that is, it is only as "we have respect for and are willing to make some sacrifice for our home organizations that the public will recognize and value the medical profession."

In their papers, addresses, and teachings they endeavored to present professional matters in such way as to be entirely impersonal, and discussed only such questions as they believed would be of benefit to the profession which they loved and in which they lived all their lives. They held to the tenets of the American Medical Association, for they believed that, since this organization represents the profession of America, it should have the support of members of the profession. They were attentive to the recent trends, believing that the attitude of the profession toward socialization of medicine is one of sincere desire for information, to learn in what way their activities can be adjusted to inevitable social changes as they come, only hoping that the quality of medical care which the profession is capable of rendering today will not be lessened.

As teachers William J. Mayo and Charles H. Mayo early recognized that an adequate training in general diagnosis and a firm groundwork of instruction in fundamental fields were essential to sound surgical practice. In the operating room they were actuated by a genuine desire to give opportunity for development to their assistants, to permit them to participate in the operations sufficiently not only to become familiar with the principles of surgery, but to acquire adequate technical skill.

The purpose and manner of their teaching in the early years culminated in the Mayo Foundation for Medical Education and Research. The training provided by the Foundation in the last twenty-five years has been based on the general plan followed by Dr. William J. Mayo and Dr. Charles H. Mayo for the many years preceding the establishment of the Foundation and its affiliation with the University of Minnesota. They gathered assistants about them, not primarily to secure aid in surgery and clinical medicine, but because they had a real de-

As I write, my mind goes back to the early days of a half-century and more ago, when the Clinic had its origin largely as the result of the cyclone of 1883 which passed over the town of Rochester, Minn. The history of the subsequent progress and development of the Clinic strongly reflects the rugged character of the early settlers, who, as a result of their training in the school of experience, were accustomed to meet and overcome the difficulties inherent in the primitive life of the great West.

In reviewing the work that the Clinic has done, it is extremely difficult to evaluate at their true worth the various elements that have contributed to make it what it is. The idea of establishing such a clinic seems to have originated in the fertile brain of the senior Dr. Mayo, but it was taken up very early by Dr. Will, ably seconded later by Dr. Charlie. It wasn't long thereafter before the name of Mayo began to be on the lips of surgeons everywhere and to appear prominently in medical journals and on the programs of surgical societies all over the country. The attractive personal characteristics of the Mayo brothers made them exceptionally welcome in any surgical gathering. The authoritative character of their scientific papers and discussions was such as to command general attention. Before long the eyes of the surgical world were turned toward Rochester, and in course of time it became the surgical Mecca of this country.

I can recall with great satisfaction my first visit to the Mayo Clinic in the early nineties. The character and amount of work done here in this prairie town were most impressive. The two brothers were, each in his own way, most interesting characters, and their devotion to each other was a pleasure to see.

As is usually the case, after starting out in the traditional way of doing everything that offered, they early began to specialize more or less in their work. Dr. Will devoted the most of his time and attention to the abdominal organs, while Dr. Charlie was a sort of all-around specialist, however, perhaps devoting most of his attention to the treatment of the various types of surgical diseases of the thyroid gland. The wealth of material furnished by the Clinic along these, indeed along all, lines enabled the Mayos to speak with the authority of wide experience upon many subjects. One had but to visit the Clinic and study it in operation to see the crowds of patients who regularly flocked to its doors; to spend a few days in the operating rooms and wards, to attend the various conferences and demonstrations of pathologic specimens, to be impressed with the value and extent of the work done by it and the power for good along all lines of professional endeavor that it was capable of exerting, and did exert, upon the profession at large. No wonder then that under the skillful guidance of the Mayo brothers there was developed out on the prairies a medical center which became the wonder of the civilized world.

A PERSONAL APPRECIATION OF THE MAYOS AND THEIR WORK

J. M. T. FINNEY, M.D., BALTIMORE, MD.

I HAVE been asked by the editors of *SURGERY* to prepare something personally reminiscent of the Mayo brothers and the splendid work done by them. This is indeed a difficult, though pleasant, task that has been set me, not only because of the extraordinarily attractive personalities presented by these two devoted brothers, but also because of the unusual character and wide extent of the work accomplished by them in their busy lives. It will be impossible in the short space allotted me to give anything like an exhaustive account of what they and their associates in the Mayo Clinic have accomplished, or what it has meant to the medical and surgical professions at large. I shall not attempt, therefore, to do more than refer to a few of the more outstanding contributions as I see them that have come out of the Clinic, and to appraise as best I may the effect that this unique institution, during its more than one-half century of activity under the guidance of these two extraordinary brothers, has had upon the progress of medicine and surgery.

In the recent death of the Mayo brothers, William James Mayo and Charles Horace Mayo, the world of surgery has suffered a grievous loss. In their work they were always so closely associated with each other in the minds of their friends and associates of the profession that it is impossible to think of one without the other. The example which they have set in devoting their lives to the betterment of their profession is certainly one for succeeding generations to emulate. Not only did they witness in their lifetime the phenomenal development and growth of modern surgery, but they themselves contributed to it in large measure.

Aided and stimulated by their remarkable father, William Worrall Mayo, they brought about a new development in the practice of medicine and surgery; namely, the gathering together of a group of men well trained in the different departments of medicine, and the establishment with their aid of a Clinic for the twofold purpose of studying and treating diseases of all kinds and of training physicians and surgeons along scientific and practical lines. Their Clinic, a model of its kind, has contributed greatly to the science and art of surgery. The Mayos have shown what can be accomplished by means of thorough organization, careful selection of capable and well-trained personnel, and unflinching perseverance in the pursuit of an ideal. Anyone who has visited Rochester, Minn., and has familiarized himself at all with the character and extent of the work done there must have been deeply impressed by what has been accomplished.

THE MAYOS AND THEIR WORK

GEORGE CRILE, M.D., CLEVELAND, OHIO

DR. WILLIAM J. MAYO and Dr. Charles H. Mayo came of a line of physicians which had extended back to the middle of the seventeenth century. Their father, Dr. W. W. Mayo, was an outstanding physician and surgeon who had been instructor in chemistry and physics at the Bellevue Hospital Medical School before receiving his medical degree from the University of Missouri. During the Civil War he was provost surgeon for Southern Minnesota and in charge of recruiting stations. In 1863 he moved to Rochester, Minn., which was to become a world mecca. With the indefatigable and progressive spirit manifested later by his distinguished sons, Dr. W. W. Mayo took a postgraduate course in medicine and became a leader and organizer of local and national medical societies. He was also the founder of St. Mary's Hospital which has played so prominent a role in the development of the Mayo Clinic.

William J. Mayo graduated in 1883 from the University of Michigan Medical School and his brother, Charles H. Mayo, graduated in 1888 from the Medical School of Northwestern University in Chicago. As the inclination of each was toward surgery, they began their surgical experience under their father's guidance at St. Mary's Hospital in Rochester.

From the very beginning the active personality of Dr. W. W. Mayo had appreciated the advantage of the association of the practicing physician with the practicing surgeon. His feeling as to the importance of this conception in general diagnosis was emphasized by his association with the practicing surgeons of his time. Thus, the "group" idea really originated with Dr. W. W. Mayo.

To me, as I knew Dr. W. W. Mayo in his later years, his spirit was well illustrated by the fact that in his eighties he took a trip to Japan alone, "to keep from getting rusty," as he put it. It is my impression that had he started where Will and Charlie began he would have had a similar brilliant career—considering his originality, vitality and his appreciation of group practice.

Dr. W. W. Mayo's two sons as students assisted him with his patients and with minor operations. He chose for them two excellent medical schools; after their graduation they began to practice with him, so that no small part of their clinical training and of their impressions of the value of group practice they derived from their father's practice.

It will be of interest to compare the state of the science and the art of medicine in 1883, when the elder of the two brothers began his practice, with the general status of the United States then. At that time the total population of the United States was in round numbers, 50,155,000; Chicago had a population of 503,000; New York City, a

As additional evidence of the type of men the Mayos were, they were not spoiled by their success or the many honors heaped upon them by institutions of learning both in this country and abroad. They remained to the end always the same charming, approachable, human men, a delightful stimulus to their professional friends, a tower of strength to their patients, and benefactors to mankind.

While it may be true, as claimed by some, that their individual contributions to scientific surgery were not outstanding, still it is an open question as to which confers the greater benefit upon mankind, the simple discovery of a scientific fact or the practical application of that fact to human needs and the popularization of it so that the greatest good therefrom will come to the greatest number. Although it is undoubtedly true that sufficient time has not as yet elapsed to afford a true perspective as to the lasting effect upon the practice of surgery of the contributions of the Mayo brothers, time and accumulated experience will determine the true verdict. Meanwhile, informed members of the medical profession, surgeons in particular, are confident that the progress of surgery as a whole has been tremendously advanced by the judicious testing of the newer methods and by the mature judgment of the Mayo brothers.

For many years the Mayo Clinic has furnished, as it were, a Supreme Court for estimating the real value of the various new surgical procedures suggested from time to time. What a satisfaction to a young, inexperienced surgeon to know that a certain surgical procedure has the approval of the Mayos! With how much greater confidence and assurance he attacks his problem! Along the special lines indicated above, the brothers have each made substantial contributions to our knowledge of the subjects treated. The mistaken idea that seems to prevail in certain quarters that surgical research is confined to operating upon animals has been largely disproved by what has been accomplished in the Mayo Clinic. The additions to our knowledge as to the causation, clinical history, the simplification and perfection of the operative technique in the treatment of the surgical affections of the gastrointestinal tract and the thyroid gland, to mention only two subjects, are such as to establish beyond question the research value of the work done by them. The impression that has been made upon the practice of medicine and surgery by the Mayo brothers through the Clinic established by them has been far reaching, and its beneficent effect will be lasting for generations to come.

tions for carcinoma, the opening of the skull for tumor, the removal of diseased kidneys. A little later the Mayo brothers took part in the opening of the field of goiter and neck surgery, the field of surgery for peptic ulcer, and the extension of plastic surgery. They also had the adventure of seeing the development and extended application of local and general anesthesia, blood transfusions, the prevention of shock, and the better preparation of patients to withstand surgical operations.

Dr. W. W. Mayo died in 1911 happy in the knowledge that during his lifetime the groundwork laid by Pasteur and Lister had permitted the development of brain surgery and cancer operations to such a point of safety that these difficult procedures could be undertaken with the same amount of ease as a hernia operation was handled during the days of his earlier practice.

It had been the good fortune of the Mayo brothers to travel widely in America and abroad and thus to bring back new ideas to their Clinic. They early applied the principle initiated by their father of associating themselves with men skilled in diagnostic methods. They, and the other men who shared this period, had the privilege of rising with the tide of immigration and increasing wealth, together with the upward spiral of advancing medical discoveries. And with this they were able to see the extension of the principle of group practice in many parts of the United States and especially in the development of their own Clinic in Rochester, Minn.

In view of the fact that agriculture and industry have reached a more stable condition and in view of the fact that their progression has not quite so much room for expansion compared with the enormous advances made since 1883, it is not probable that an advancement equal to that of the last fifty years can be expected in the coming fifty years as far as surgery is concerned. The great advances will be in internal medicine and in a better understanding of the physical nature of the animal mechanism through physics and chemistry. With this better understanding of the physical nature of the animal mechanism will come a great expansion in the field of preventive medicine.

The Mayo Clinic Foundation in the past has been a leader in the application of each new advancement in the entire domain of medicine, surgery and its specialties. The Mayo brothers have generously contributed in research to the art and the science of medicine in their period of activity and have set up an endowment fund to perpetuate their work. During their lifetime they contributed to the sick man of today, and in their perfectly organized Medical Clinic they are contributing aid to the sick man of tomorrow. This constitutes a great memorial, not only to Dr. William J. Mayo and Dr. Charles H. Mayo but also to their father, Dr. W. W. Mayo.

population of 1,911,000; and Cleveland, a population of 160,000. At the present time the population figures have jumped to 129,257,000 for the United States; 4,364,000 for greater Chicago; 7,960,000 for greater New York, and 1,271,000 for greater Cleveland. With this growth in urban population the Mayo Clinic with its rural setting kept pace.

Thus the vigorous seedling of group practice planted by Dr. W. W. Mayo was fostered and nursed by his two famous sons, not only under the most rapid development and expansion of the United States through the tide of immigration which has continued to rise until the present time, but also under the most rapid development in the science and in the art of medicine.

It should be remembered that, when Dr. W. J. Mayo graduated from medical school in 1883, anesthesia was in its infancy, for, although anesthetics had been administered since 1846, the favorable and unfavorable indications for the depth of anesthesia under varying conditions were but little understood.

Only sixteen years before Lord Lister had published his revolutionizing treatise, *On the Antiseptic Principle in the Practice of Surgery*, which converted the operating rooms of that time from pestilential chambers to the aseptic perfection they now represent. At that time a carbolic spray was used freely in the operating room, and septicemia and wound infections were such a menace that the skull, abdomen, bladder, joints, bones, and spinal cord could not safely be operated upon. To be sure the abdomen was opened and a limited range of operations was performed, but infection often proved fatal. Surgery then was largely devoted to the care of accident and emergency cases; at that time there were almost no cases of cured carcinoma of the breast or uterus.

The entire medical practice in the 1880's was sharply divided into either general medicine or general surgery, with none of our present-day specialization. The general medical man took care of pediatrics, obstetrics, and psychiatry, while the general surgeon corrected deformities, set bones, operated upon the urinary tract, removed tonsils and adenoids, and removed injured eyes. The Mayo brothers were such general surgeons, their practice consisting of attending whoever was sick whether the problem was surgical or not.

In the 1880's and 1890's there was no neurosurgery and no genito-urinary surgery; all the specialties were taken over by the general surgeon. So, Dr. W. J. Mayo and Dr. Charles H. Mayo in common with McBurney and Bull (New York), Richardson (Boston), Keene and Gross (Philadelphia), Halsted and Finney (Baltimore), Murphy and Ochsner (Chicago), Huntington (San Francisco), and Matas (New Orleans)—in common with all of the men of this period, they enjoyed the thrill of excitement in the opening of the various fields: the surgery of the abdomen, the removal of pus tubes, the various opera-

benefited from this form of treatment; and (4) the recent experiments emphasizing the tremendous roles that minute quantities of chemical substances, known as hormones or vitamins, may play in life—all give evidence that modern medicine is indeed one of the most brilliant movements in applied science.

Whether this public interest is something deeper than curiosity and whether it can be relied upon as a potent factor for the common good have not been demonstrated. Indeed, a study of the historical background of surgery invokes in the mind of the medical scientist a distrust of the public. One has only to recall the many great figures of science who were either scorned by the people or actually tortured, because their discoveries, soon to benefit mankind, seemed at the time unorthodox. It may not be common knowledge that Michael Servetus, who discovered the pulmonary circulation, was burned at the stake along with all his books because he dared to state the truth. And we have only to mention that during the Middle Ages the Church frowned upon anatomy and surgery, and that the Edict of Tours (1165, *Ecclesia abhorret a sanguine*) declared surgery was not respectable. The feeling became so strong that the School of Medicine at Montpellier issued a decree that none of the students should practice or study surgery.

Even recent American medical history is replete with incidents of how the public attitude erected barriers to progress. It should be common knowledge that Dr. Zabdiel Boylston, of Brookline, Mass., when he first inoculated a man for smallpox, was chased by a mob, and that his life was threatened so that he had to hide in his house. The early history of the Harvard Medical School is a good example of the dangers involved in teaching medicine. Obviously, anatomy had to be taught, if the public were to receive the benefits of good medical practices; yet bodies were not procurable. Grave robbing was resorted to, causing difficulties with the police which have been vividly described by J. C. Warren,¹ later to become Professor of Surgery and Anatomy. His experiences emphasize how greatly public opinion is influenced by sentiment, not reason, and how such a sentimental view may impede progress.

Less than a century ago there was no anesthesia in the modern sense; bacteria, as the cause of infectious diseases, were unknown; and medicine, as we know it today, did not exist. In 1846 ether was discovered and given to the world (chloroform appeared the next year). Then the "dark days of medicine" ended, only to return to confound and terrorize both physician and patient as operations were followed by infection. To be sure, men could be put to sleep, and the terrible disorders from which they suffered could be removed painlessly with the knife or the canter. But this gift of anesthesia proved at first a curse, for man did not understand at this time that bacteria lurked everywhere. The doctor did not know that his instruments carried filthy organisms, and therefore death, to his patient. The slightest use of the scalpel

PUBLIC OPINION AND ANIMAL EXPERIMENTATION

ELLIOTT C. CUTLER, M.D., BOSTON, MASS.

What is it to have lands and houses, to abound in silver and gold, to be decked with pearls and diamonds, yes, and to possess the whole world, to rule Nations and countries, and to lack health, the chiefest jewel and greatest treasure of man's life and delight.

—*Thomas Vicary*, 1548.

THERE could be no more appropriate place for a discussion of animal experimentation than in a collection of papers dedicated to the brothers, William and Charles Mayo. Their good deeds for suffering humanity, every fragment of their life's work, and the very pedestal on which their success depended were derived from animal investigation. It is time that every doctor took up the endgels in defense of experimental medicine and explained to the laity how the advances in the healing art have come about largely through the use of animals. In particular, it should be understood that the science of bacteriology is the very basis of surgical practice. Before the advent of bacteriology, surgical operations were attended with almost inevitable sepsis, so that hospitals came to be looked upon by suffering human beings as places definitely unhealthful for them to enter. With the coming of the study of bacteria as the cause of infection and with slow and continuous animal investigation, which proved not only how bacteria cause disease in living matter but how the bacteria can be killed off so that infection is not passed from individual to individual, came the first steps in modern surgical advance. On these animal investigations are securely erected our present methods of sterilization. Without such methods, the surgery of today could not exist. It would appear that these facts are not widely disseminated among the public.

The extraordinary interest of the news-reading public of today in scientific matters is an excellent gauge of the spread of education to all classes of our people. This general inquisitiveness for scientific knowledge has led to a special interest in those matters dealing with public health and, indeed, with all medical affairs. Man, having spent centuries discussing his soul, has at last become interested in his body.

There appears to be some justification for this special interest in modern medicine, for (1) the great extension of life in recent years, due largely to man's knowledge of the role of bacteria in infectious diseases and hence of how to avoid infections; (2) the recent successful attacks on other types of disease, as seen in the present methods of treatment for diabetes and pernicious anemia; (3) the rapid progress of surgical therapy to the point where a majority of our citizens have at some time

This brief recital of the advance of medical progress is but a promise of the future. Do our people know why, in the graveyards of New England, so many wives lie beside one husband? Do the rows of little stones about the headstone of a family mean nothing? The history of bacteriology is available to all. Can they envisage their great-great-grandfathers strapped to a wooden table and writhing in pain whilst the best surgeon of that day groped in his dirty bag for the knife with which he opened the bladder for removal of a stone that made life a hell on earth? The blessing of anesthesia has done away with all this suffering. Why is it that so much smugness settles upon a comfortable people? Our citizens avoid these terrible calamities because scientists have toiled in the night against the same complacency that now encompasses this generation. Our ancestors made laws that made the proper study of disease a crime. Bodies were not allowed for dissection, and the use of animals was decried. A few saw the light of greater comfort and happiness, and struggled on, criticized by the "good people" of their day, chased by the police, and blasphemed by those they sought to help. These few had to rob graves of their occupants in order to teach the next generation enough anatomy to bring comfort to our generation. Experiments upon animals were surreptitious affairs.

The laity will smile at this recital of earlier days, but are they really helping their own generation and the generations to follow in any better fashion? Do they know where the bodies needed to educate those who are to care for their children come from? Each year the number available decreases. The coroner takes the bodies of the criminals and every accidental death, even if he does not examine them. The State Hospital official is afraid of criticism if he gives up bodies, even under the law. In at least one state a law has even been proposed that the state give proper burial to unclaimed people, a move which would destroy even the meager supply now remaining. Soon the young doctor will have to learn his anatomy on living bodies, i.e. his patients! And as for animals—over 50,000 are sacrificed each year by a single Animal Rescue League, while the scientists must pay great prices for strays brought to them. One can properly state that about \$1,000,000 is paid out each year for animals used in research laboratories in the U.S.A., while a hundred times more animals than would be required are put to death by Animal Rescue Leagues, etc. Thus, \$1,000,000 a year which might be devoted to the care of human suffering is needlessly expended.

How does this come about? Because the healthy citizen neglects his duty of citizenship and allows a misguided minority to inject sentiment into our laws, to set aside reason, and thus to jeopardize his health and the health of his family. Each year new laws are proposed making the use of animals for scientific purposes more difficult. Each year workers in laboratories must stop work and tie themselves to Committee Rooms in the State Houses of our country, there to be maligned as cruel mon-

meant grave infection. Women put to sleep to ease their pains during childbirth were infected by the doctors who sought to bring them comfort. No wonder that in those times people looked askance at hospitals and feared to go to them!

It was a full thirty years more before the discovery of bacteria by Pasteur and Koch and the application of their discovery to surgery by Lister taught the medical profession that, if they would make progress, they must study bacteria; they must find out how bacteria give rise to diseases; and they must learn how to rid the operating rooms and the hospitals, as a whole, of bacteria. The innumerable experiments upon animals necessitated by these studies undoubtedly resulted in suffering for a great many creatures. We should not hide the fact, but now we, who benefit from these studies, should make acknowledgment both to the animals, who have made our lives safer and more comfortable, and to the investigators, who had the courage in the face of hostile and bitter criticism to carry forward their works. We should not have known how to sterilize all the materials used in operating rooms today, unless we had found out upon animals what organisms did when they entered a living body. Thus, every person today whose life has been saved or made more comfortable through a surgical operation owes a deep debt of gratitude to the animals concerned with this development. One should not deceive people. Though there be those who object perhaps to what has gone before, they must be willing to balance against these experiments on animals the thousands of children saved from diphtheria and the countless lives made comfortable through surgical operations for acute appendicitis, strangulated intestines, or tumors of the womb.

Not only has man benefited from these experiments, but the animals themselves have benefited. Texas fever, which at one time destroyed a great part of the cattle bound for the meat markets, has now disappeared because Theobald Smith used a few animals in studying the transmission of the disease from steer to steer through a tick. Similarly, hog cholera, which decimated swine, is now under control because of a few animal investigations. The foot and mouth disease, through a similar group of experiments, has practically disappeared from this country. Indeed, experiments made to protect animals have frequently resulted in benefit to man. Thus, the drug which Maurice Hall found would cure hookworm disease in dogs later proved effective in man and alleviated the suffering of millions of our own genus in the South. And what of the beneficial and helpful surgery now performed on horses, cows, and dogs for their own good and comfort? The great good to animals that goes on in the many splendid animal hospitals set up by Humane Societies could not exist unless the role of bacteria in relation to infection had been discovered by animal experiments. Think of the protection to animals given by vaccination for rabies, for horse encephalitis, and for distemper!

ner upon patients in hospitals. Neither investigators in the laboratories nor the doctors in the hospitals give anesthesia for the taking of blood specimens, for the passing of a stomach tube, for a lumbar puncture, or for like procedures. Moreover, further control exists by reason of the fact that no editor of a reputable medical journal will publish the results of experimental work if cruelty to the animals has unnecessarily occurred. And the profession of medicine itself frowns on work that does not protect carefully the experimental animals.

With this understanding we propose that the time has come for the more intelligent application of scientific labor for the improvement of our health and comfort. We need a law that gives unclaimed animals without cost or quarrel to reputable centers for medical study, such as our medical schools. Thus, at no financial outlay an adequate supply of animals would be available, funds previously spent for the purchase of animals would be released for greater efforts in combating disease, and those who labor daily for the public good would be encouraged to greater efforts by this attitude and this assistance. Further, the laws concerning unclaimed bodies must be changed in some states, making it mandatory with state institutions to turn over unclaimed bodies to the already prescribed institutions. Thus will a beneficial impulse be given to the betterment of public health.

REFERENCE

1. Warren, Edward: *The Life of John Collins Warren, M.D.*, Boston, 1860, Ticknor and Fields, Chap. XXVI.

sters, in order to defend the present laws and to prevent the passage of new laws that would make fruitless the continuance of their efforts for the relief of suffering. The people who attempt such changes in laws often wear feathers, plucked in some instances from living birds; they eat meat which is more tender because a farmer without an anesthetic removed a part of the animal's body with a knife, when the animal was young; they often wear around their necks furs secured from animals trapped in the north and allowed to freeze to death with a leg broken in a steel trap. Fur trappers have stated that, for every fur brought in from traps, two to five other animals have been eaten from the trap by predatory birds and beasts. And they call scientists cruel! All the laboratory experiments of the last fifty years have not caused as much suffering as the preparation of meat for our markets in a single year!

The use of animals in laboratories is carefully protected. The following rules hang in each reputable laboratory in the United States and are carefully enforced. These rules are based on the principle that animals in laboratories shall be afforded the same care that is given patients in hospitals and that the infliction of pain shall be avoided in the same manner as it is in hospitals.

RULES REGARDING ANIMALS

I. Vagrant dogs and cats brought to this Laboratory and purchased here shall be held at least as long as at the City Pound, and shall be returned to their owners, if claimed and identified.

II. Animals in the Laboratory shall receive every consideration for their bodily comfort; they shall be kindly treated and properly fed; and their surroundings shall be kept in the best possible sanitary condition.

III. No operations on animals shall be made except with the sanction of the Director of the Laboratory, who holds himself responsible for the importance of the problems studied and for the propriety of the procedures used in the solution of these problems.

IV. In any operation likely to cause greater discomfort than that attending anesthetization, the animal shall first be rendered incapable of perceiving pain and shall be maintained in that condition until the operation is ended.

Exceptions to this rule will be made by the Director alone and then only when anesthesia would defeat the object of the experiment. In such cases an anesthetic shall be used as far as possible and may be discontinued only as long as is absolutely essential for the necessary observations.

V. At the conclusion of the experiment the animal shall be killed painlessly.

Exceptions to this rule will be made only when continuance of the animal's life is necessary to determine the result of the experiment. In that case, the same aseptic precautions shall be observed during the operation and as far as possible the same care shall be taken to minimize discomforts during the convalescence as in a hospital for human beings.

Thus, operations upon animals are conducted under anesthetics exactly as operations upon man, and the animals are equally well cared for. I know of no laboratory experiments on animals done today without general or local anesthesia which would not be done in the same man-

and operations directed to relieve them are more readily undertaken by the surgeon. That any surgical procedure can be devoid of all danger is still a hope of the future; on the other hand, the evidence for or against elective surgery must be carefully weighed. An operation in the early stages of biliary tract disease often forestalls an urgent surgical need that may come in later months or years. This unavoidable surgical problem may be ten times as dangerous as an operation at a time of election and before the disease has caused damage to the liver, pancreas, and other neighboring structures. These factors have brought about an increase in operations on the gall bladder and ducts as soon as evidence is clear that these are diseased. Thus, it is important that these operations be undertaken in such a manner that fatalities will be rare and serious damage to vital structures will not often take place. One of the most tragic surgical accidents is injury of the common duct during cholecystectomy. These patients often do not die soon after the operation but remain alive as invalids for years. Restoration of the duct continuity becomes increasingly difficult as the weeks of hopeful waiting pass by.

This leads me to stress an operative technique that will be associated with very rare injury of the common or hepatic ducts or an accidental ligation of the hepatic artery. There are many anomalies of the ducts and, occasionally, the hepatic artery actually crosses the surface of common hepatic duct in a diagonal direction. In the dissection required to expose the cystic artery and cystic duct, there often occurs some bleeding; this may obscure the anatomy of this region to an extent that structures are mistaken one for the other. It is obvious one should never clamp and divide any vessel or duct under any circumstances that fail in the accurate identification of the cystic duct and artery and the common hepatic duct. In fully 50 per cent of the patients who are operated upon in the Massachusetts General Hospital for biliary tract disease, this dissection cannot be made with accuracy and safety if this part of the operation is undertaken while the gall bladder is still in place. Varying degrees of inflammatory reaction in this region and the contour of the patient account for this difficulty. That an experienced surgeon may safely make this dissection in nearly every instance without damage to nearby structures is admitted. That this is the method of cholecystectomy which should be taught, as the correct one, to younger surgeons is strongly questioned.

Cholecystectomy from the fundus toward the ducts is an old procedure. As a matter of fact, probably all of the early operations were carried out in this manner. Anatomical dissection from the ducts toward the fundus is a natural result of the more accurate knowledge of anatomy by the operating surgeon and his correct effort to secure the blood supply before the removal of any part. When exposure is ideal, this type of operation simplifies the procedure of cholecystec-

THE SURGICAL MANAGEMENT OF THE USUAL EXTRAHEPATIC BILIARY LESIONS

ARTHUR W. ALLEN, M.D., BOSTON, MASS.

(From the Surgical Service of the Massachusetts General Hospital)

SINCE the early days of elective surgery, diseases of the gall bladder and bile ducts have afforded the surgeon many interesting problems. The first bold attempts were directed toward the simple drainage of an acutely swollen gall bladder with the removal, if possible, of the stones within it. With the advent of satisfactory anesthesia, these operations were gradually replaced by extirpation of the inflamed structure. As surgical asepsis and technique improved, the interval removal of a gall bladder containing stones that had produced recurring attacks of inflammation or even colic became a common practice. The safety of simple drainage as opposed to cholecystectomy was a chief source of debate among surgeons a little over a quarter of a century ago. That those patients who survived the more radical operation were more likely to remain symptom free than those who had simple drainage was soon established. It did not take long to reverse the mortality figures since the drainage operations were reserved for the very ill or feeble patient, while cholecystectomy became a routine practice whenever feasible.

Operations on the common hepatic bile duct were undertaken only when symptoms and signs developed indicating a stone in the duct. These were usually after cholecystectomy had failed to bring relief and, practically, the only indication for duct exploration was jaundice that had followed biliary colic. As time and experience progressed, it became obvious that other signs and symptoms were indicative of duct pathology. We are now faced with the problem of exploring the ducts in a considerable proportion of primary operations on the biliary system. It has been shown that approximately 20 per cent of all patients now operated upon for stones or inflammation in the gall bladder also will have stones in the bile ducts. That many of these stones are small and pass through the papilla of Vater with or without pain is well established. It has been recognized, however, that the chance of having these duct stones produce symptoms requiring further surgery is likely. For this reason, the ducts should be explored at the primary procedure if the indications of trouble within them are evident; these are based on the history and physical signs present before operation, as well as the findings at the time the region is exposed.

Since diagnostic methods¹ have progressed to a point where positive evidence of biliary tract pathology can be made by the roentgenologist, operations at a time of election have become more frequent. Patients are now more willing to submit to elective surgery

during certain phases of inflammation. Having this in mind, it occurred to Rowley³ to use artificial edema in the peritoneal covering of the chronic gall bladder and thus make the dissection easier. The principle for this aid in separating delicate tissues was probably first advocated by Bevan⁴ in his article on the technique for operation on the undescended testicle. I have found this method so successful that now cholecystectomy from the fundus toward the ducts is a simple and satisfactory procedure; rarely is there any break in the continuity of the underlying muscular and mucous coats so that the operation progresses in an orderly fashion. Having freed the gall bladder well down to the ampulla and secured the venous communications, one then places a moist gauze pad in the liver bed and, by retraction in two directions, exposes the duct area accurately. Danger to the common duct and the hepatic artery is thus reduced to a minimum, since they are approached and visualized as they are directly exposed from above.

We have attempted to trace the type of operation done in every instance of damage to the common duct that has entered the Massachusetts General Hospital. In only one patient in this group was the duct injured when the operation had been carried out from the fundus toward the ducts. This indicates that the procedure we recommend is not entirely devoid of danger but that catastrophes are less likely to occur. It has been frequently stated that the questions of courage, knowledge, and skill are all at stake if one deviates from the so-called anatomical operation of cholecystectomy from the ducts toward the fundus. This attitude has caused many young surgeons to make an error in judgment in the presence of inflammatory reaction that would challenge the most experienced man in this field. Little has been said in recent years concerning a safe and orderly operation carried out as described above. We feel that it is wise to teach this method to the resident staff and urge them to carry out this procedure in easy cases at first, so that the technique will not be difficult for them when they are faced with the deeply placed, adherent, or inflamed gall bladder.

In our clinic there has been a run of 432 consecutive cholecystectomies in the past four years with 7 deaths, a mortality rate of 1.6 per cent. In the previous five-year period there were 22 deaths in 751 cholecystectomies, a mortality rate of 2.9 per cent, giving an average mortality rate for nine years of 2.45 per cent. Common duct explorations were carried out in conjunction with cholecystectomy in 35 per cent of patients operated upon between 1931 and 1939. During the past four years, this figure rose to 44.2 per cent. In this latter group stones were found in the ducts in 20.7 per cent of all the patients operated upon or less than one-half of the ducts explored. About 6 per cent more of these were found to have an abnormally tight sphincter of

tomy. Division of the cystic artery decreases the bleeding during the remaining dissection. Unfortunately, such a procedure frequently results in the removal of that portion of the fibrous capsule of Glisson that protects the liver. If this is lost, closure of the raw liver surface is difficult and there is considerable seepage from small bile sinuses as well as from veins in this area. It is easy to forget that there is no cystic vein accompanying the artery. The venous return from the gall bladder is through multiple small veins going directly into the liver. The need of attention to the liver bed has caused Thorek² to recommend leaving the entire thickness of the gall bladder attached to the liver and destroying the mucous lining of this remaining segment by electrocoagulation. This, and other papers on the subject, would lead one to believe that it may be the usual custom of some surgeons to denude the liver bed when removing the gall bladder. It has long been a practice in our hospital and elsewhere to carefully preserve enough of the posterior serous coat and the fibrous capsule directly between the gall bladder and liver surface to peritonealize adequately this defect. This refinement is of great importance since often, when neglected, the duodenum becomes firmly fixed to this raw area by dense adhesions. Not only will such a complication frequently cause serious digestive symptoms, but the hazard of any future operation in this region is increased. I am convinced that this area should be left dry and that careful peritonealization is to be accomplished at all costs. This can be more easily arranged if the dissection is carried out from the fundus toward the ducts. The objection to the method is increased bleeding during the operation; this can be easily controlled by a painstaking ligation of the venous channels as they are exposed. Also, when small stones are present in the gall bladder, they on occasion may be forced through the cystic duct during the necessary manipulation of the gall bladder. It is often possible to isolate the cystic artery and duct at the beginning of the operation and place upon them temporary clamps. This obviates most of the objections and it immediately occurs to everyone that, having done this, why not carry out the dissection from below upward. The reasons are chiefly that in many instances these clamps will be found too near or too far away from the common duct and that actually they have not been placed where they should be for best results. Also, as stated above, it is frequently impossible to prevent a portion of the fibrous attachment from pulling away from the liver bed. Once it is detached, there will be a certain amount of bile and blood leakage from this denuded area in spite of any effort to combat it. That such may not interfere with a successful outcome is admitted, but serious complications can arise from this source.

We have all noticed the ease with which the peritoneal covering of the gall bladder can be separated from the underlying structures

tory or operative findings are correct, we will have to expect a high percentage of negative explorations. On the other hand, we will overlook stones in the ducts of many patients who will continue to have symptoms if we do not investigate the ducts when there is reasonable evidence that a stone or a constricted papilla exists. With this in mind, we must standardize our duct explorations in such a manner that this added procedure does not increase the danger out of propor-

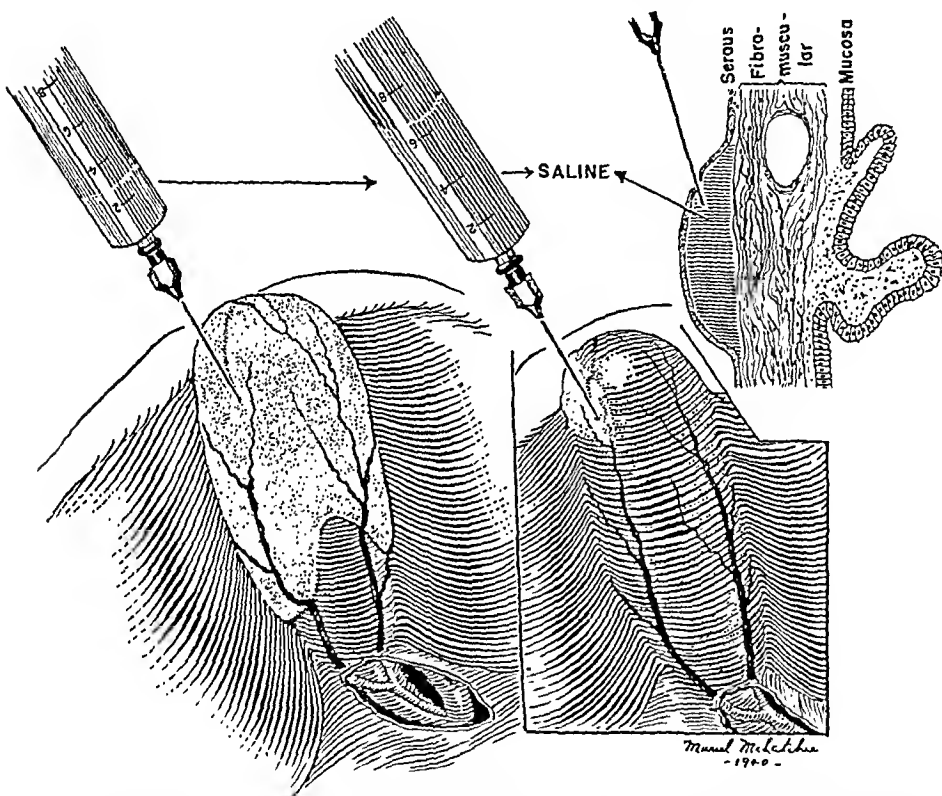


Fig. 2.—Schematic drawing to demonstrate the method of producing artificial edema of the gall bladder wall. Sterile water, salt solution, or novocain solution may be used. Temporary clamps placed on the cystic artery and duct decrease the bleeding and prevent small stones from being manipulated into the common duct during the dissection. These are unimportant features and such clamps should be cautiously placed. The inset shows by cross section a small segment of the wall of the gall bladder indicating the ideal cleavage plane in which to introduce the fluid. The artificial edema outlines the blood vessels more clearly. The incision through the peritoneal surface can be made into this edematous area with little danger of penetrating the deeper coats of the gall bladder.

tion to the rewards for such interference. In our hands this is carried out in a systematic fashion. Perfect exposure of a segment of the supraduodenal portion of the duct must be obtained. Usually, it is wise to free the outer attachments of the duodenum so that this structure can be rolled toward the median line. The duct is aspirated with a fine hypodermic needle, an important precaution regardless of the appearance of the bile withdrawn. When possible, the common duct is opened distal to the cystic duct, but there is great variation in the

Oddi. Thus, it is evident that common duct exploration was carried out about twice as often as was necessary. We have carefully studied the records in these cases to ascertain the indications for duct exploration and find it difficult to cite many instances where the procedure was unjustifiable. We did remove stones from a certain number of ducts of normal size or less when the indications were correct. In our series the most reliable symptom of common duct stone, other than jaundice, was frequency of attacks. In 66 patients who had attacks of pain as often as seven or less days apart, we found stones in the ducts

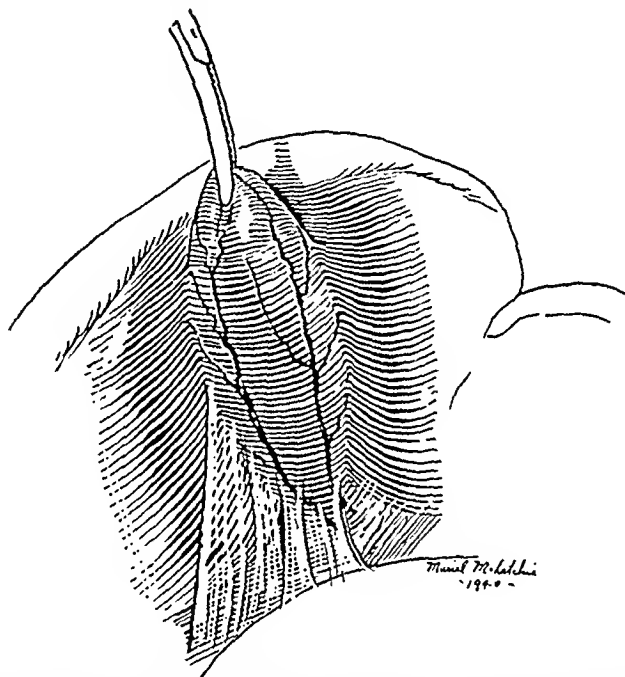


Fig. 1.—Schematic drawing representing adhesions about the lower segment of the gall bladder and bile ducts. This is a frequent finding and often under these circumstances the dissection required to expose the cystic duct and artery is accompanied by enough bleeding to obscure the field.

of 60. We are sure that one cannot depend on the size of the duct as an unmistakable criterion for stone within it. Inasmuch as the mortality rate was elevated to 4.25 per cent when duct exploration was superimposed on cholecystectomy, we felt that further analysis of this group was indicated. In those patients who had stones removed from the ducts at operation, the mortality was 7.16 per cent, while in those in whom no stones were found the mortality rate was 2.04 per cent. In other words, the careful exploration of the duct itself need not increase the risk, while the pathologic processes associated with common duct stone are significant of a more serious situation.

If we are to explore the ducts in a large proportion of routine primary operations on the biliary system, when the indications from the his-

detritus. The duets may be irrigated with normal salt solution to better advantage after the next step, which we feel is so important.

Many surgeons have felt for years that it was wise to ascertain the patency of the duct outlet. A considerable number have become conscious of the need for more than this. The gradual, careful dilatation of the papilla of Vater has become increasingly more popular. The rationale of such a maneuver is based on the frequent findings of a very tight outlet and subsequent symptoms if dilatation has been omitted. Warnings have been issued concerning the danger of such a practice, but, if it is carried out in a logical manner, these dangers are minimal.

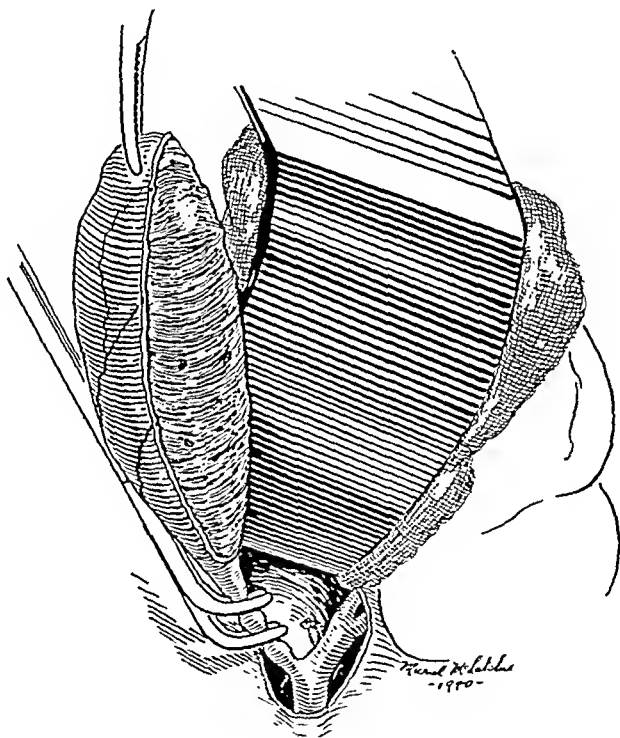


Fig. 4.—The pad protecting the liver has been moved downward so that the entire right lobe can be held out of the way. The ducts are carefully palpated for stone and great care is used not to leave a stone in the stump of the cystic duct.

In our hospital there has been a gradual adoption of routine instrumentation of the papilla of Vater whenever the ducts were explored. We have approached this feature of the operative technique⁵ with caution and after some experimental evidence indicated that serious damage did not occur. During the five-year period between 1930 and 1935, 395 ducts were explored; of these, 231 had dilatation of the papilla of Vater, while in 164 no dilatation was done. In the next four years 380 ducts were explored with dilatation of the papilla carried out in all but 50 cases. The operative mortality averaged a little over 1 per cent greater

length and entrance of this duct into the common duct. One should estimate the size of the duct and make a longitudinal incision in it not longer than the diameter of the duct itself. This wound is best held apart by fine silk guy sutures since these cause less trauma than instruments devised for this purpose. It is wise to culture the bile that escapes from the open duct since subsequent infection, if it should develop, may be more intelligently treated. The escaping bile should

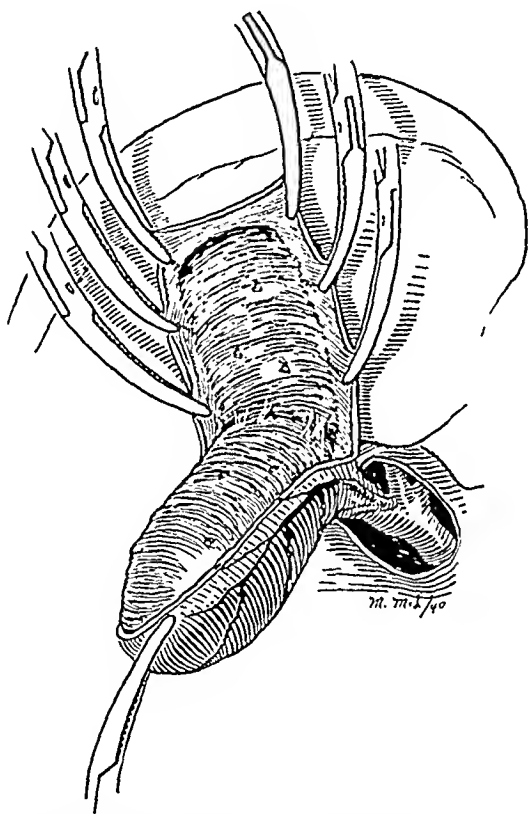


Fig. 3.—As the dissection is carried down between the muscularis of the posterior wall of the gall bladder and the fibrous capsule of Glisson, the small venous sinuses can be secured and ligated. At this point or in most instances after the dissection has been carried further toward the ampulla, a moist gauze sponge is placed against the liver and retraction made by a second assistant.

be picked up with a suction tip. I have found it of great advantage, at this stage of the operation, to go to the left side of the patient so that, by placing two fingers of the left hand in the foramen of Winslow, I can palpate the region of the ducts more satisfactorily. Instruments can be handled under vision and guided by touch. After removing the obvious stones by milking them from the ducts into the incision, one then may use long curved stone forceps to advantage. Smooth scoops or brain spoons will aid in the removal of small stones, fragments, and

in 2 instances recorded the papilla was found to be the same size to which it had been dilated at the first operation. One other patient in this group had four attacks of biliary colic after leaving the hospital but has been symptom-free for a subsequent period of three and one-half years. In the 214 patients who did not have the papilla dilated, there were 11 secondary operations with stones found in 9. Ten other patients in this group continued to have symptoms indicative of stone or dyskinesia but were not reoperated upon in our clinic. Thus, there

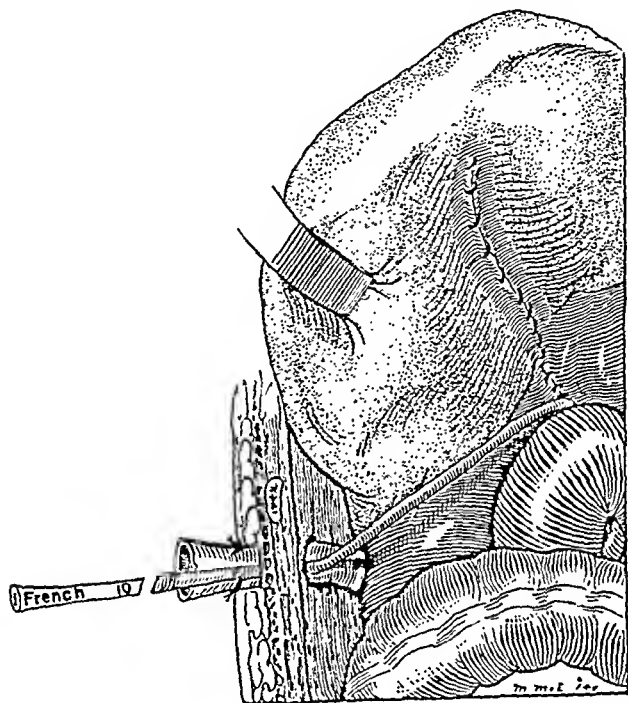


Fig. 6.—The anterior abdominal wall is left out of this sketch to give a better idea of the relationship of the wick and the tube from the common duct to surrounding structures. It is important to see that bile is draining from the common duct tube before the abdomen is closed. Stab wounds for drainage are helpful in thin patients in whom a vertical incision has been made. This additional wound should be placed well below the twelfth rib and the wick placed in Morrison's pouch under direct vision. Obese patients with a wide costal angle do better with a transverse incision.

TABLE I
REASONS FOR PROLONGED HOSPITALIZATION

| PAPILLA | DILATED (561 CASES) | NOT DILATED (214 CASES) |
|--------------------------------|------------------------|----------------------------|
| Wound sepsis | 29 | 18 |
| Pulmonary complications | 9 | 2 |
| Prolonged biliary drainage | 4 | 27 |
| Bile peritonitis | 4 | 1 |
| Study for other diseases | 4 | |
| Dehiscence | 3 | 1 |
| Miscellaneous | 8 | 5 |
| Total | 61 | 54 |
| Percentage of total operations | 10.9 | 25.7 |

in those patients not having dilatation of the papilla. This may be partially coincidence or possibly some of the patients not having dilatation were more ill and the surgeon elected to omit this procedure. The increased morbidity, however, in the nondilated group is very striking. This apparently substantiates the claim that many patients need this stretching of the duct outlet to allow for the early unrestricted flow of bile into the duodenum. (Table I.) Eight of the 561 patients having dilatation of the papilla came to secondary operation on the duct at some later period. In 4 of these stones were again found in the ducts and

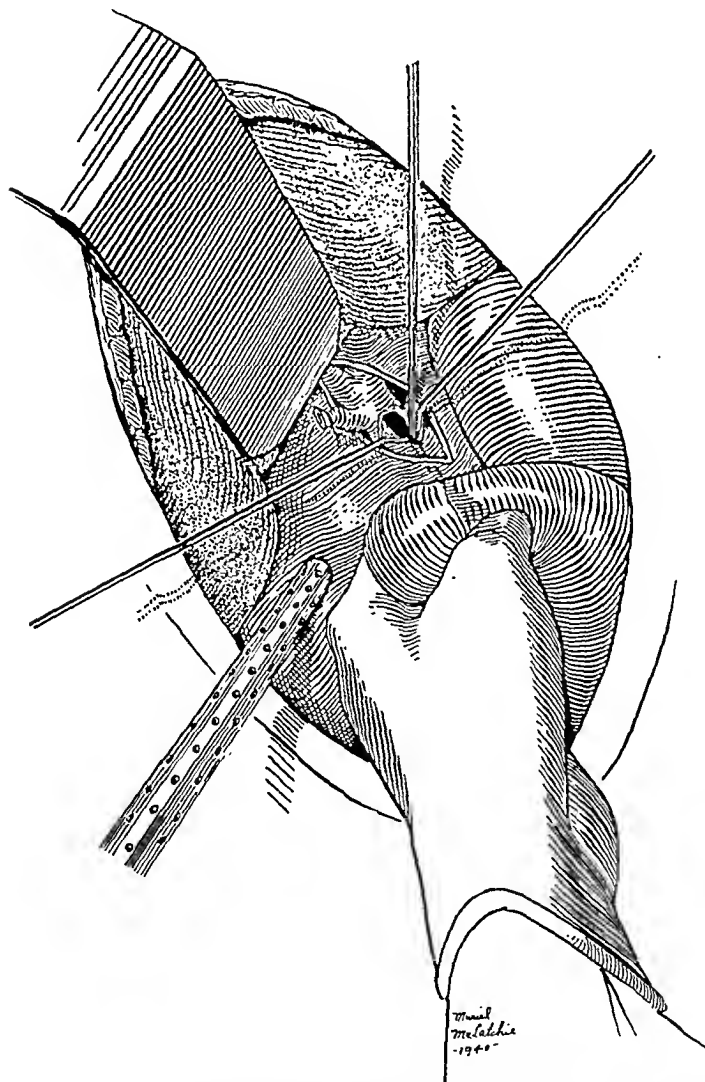


Fig. 5.—Schematic drawing indicating the method of instrumentation of the duct and papilla. The operator is standing on the patient's left. The ease of manipulation of the instruments from this position often simplifies the procedure.

had large ducts with dilatations of the outlet above the average size. We must take into consideration the fact that such individuals have liver damage and permanently dilated and usually infected hepatic ducts at the time of operation. The dilatation of the biliary tree has been a gradual process. Perhaps, they have developed a certain immunity to the bacterial flora of the upper gastrointestinal tract. Possibly, their apparent good health after operation was subjectively one of comparison to their previous state. At any rate, we found no evidence that dilatation of the duct outlet to a size comparable to that of their hepatic ducts resulted in any serious sequelae. I believe that such a dilatation is not comparable to surgical anastomosis between the duct and the

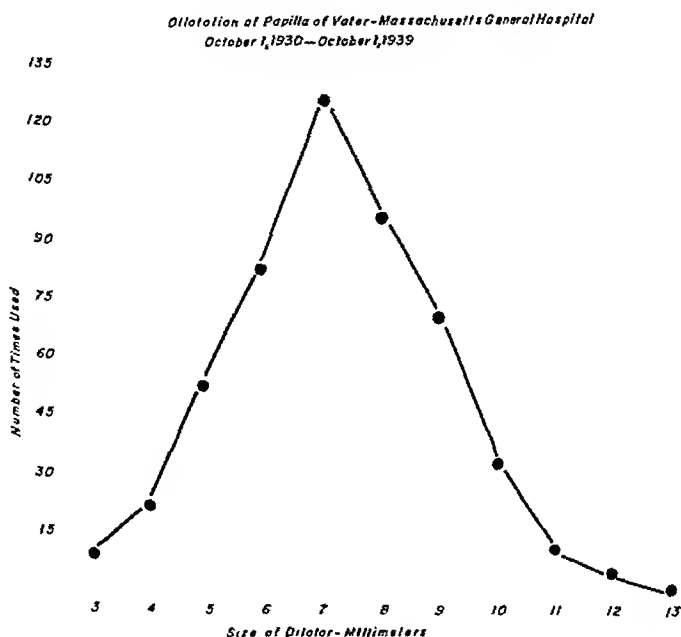


Fig. 7.—Showing the average dilatation of the papilla of Vater in 561 consecutive cases.

duodenum. In the first place, the direction and place of entrance are unchanged from those provided by nature. Also, one must bear in mind the oblique direction of the duct through the wall of the duodenum. This makes it likely that some valvelike action of the duodenal mucosa may exist after the sphincter has been destroyed.

Bakeš believed that the duct outlet remained the size to which it was dilated for an indefinite period and possibly permanently. This opinion was chiefly based on two patients in both of whom the dilatation had been carried to over 1 cm. In two of our patients having secondary duct exploration for stone, the papilla was found to admit the same size dilator that was used in the first operation. These were 8 and 9 mm. respectively. I can offer no satisfactory theory as to how stones of such

is this evidence that routine dilatation of the papilla reduces the chance of continued or recurrent symptoms from approximately 10 per cent to less than 2 per cent. In none of our cases has there been evidence of cicatricial obstruction to the duct outlet after dilatation. Duodenal reflux has occurred only once after this procedure with spontaneous recovery in twenty-one days. We have not been unfortunate enough to precipitate a serious acute ascending infection.⁶

There are a variety of methods for dilating the duct outlet. Cheever⁷ described the use of woven silk Coudé urethral catheters for this purpose. Walters and Snell⁸ prefer long, smooth, graduated scoops. Mixer⁹ has devised an ingenious hollow metal dilator which allows the injection of irrigating fluid through it. Various urethral sounds and bougies have been advocated. Bakeš¹⁰ made some elongated olive-tip metal bougies with malleable handles; these are graduated from 3 mm. upward, with each larger size only 1 mm. greater in diameter. We have found these dilators satisfactory and they have the advantage of being easily sterilized and always at hand. One should never attempt to stretch the duct itself. If the size of the duct is measured by the dilator, one should never use an instrument of greater diameter. The instrumentation of the papilla should be carried out without force and rarely should the dilatation exceed that of the estimated diameter of the hepatic ducts. The average dilatation in our cases was 7 mm. In the small-sized ducts one may wish to use the largest dilator that will enter the duct without stretching it in order to obtain the maximum opening into the duodenum. In the very large ducts one may feel that stones can remain in the hepatic ducts after all reasonable efforts have been made to remove them. In such an instance provision may be made for their passage into the duodenum by stretching the papilla to a size comparable to that of other stones found within the ducts or to that of the diameter of the hepatic ducts; occasionally, this requires the use of the larger sized dilators.

Disturbance of the sphincteric action of the papilla of Vater has been frowned upon by some investigators. It has been stated that serious sequelae, such as indigestion and ascending infection, may occur. Comparison has been made between this disturbance of the sphincter by dilatation and the results obtained following surgical anastomosis of the duct to the duodenum. We have considerable clinical evidence that the average dilatation of 7 mm. does not produce either of these complications. Cheever felt that the human papilla could be gradually dilated to this degree without permanent interference with its function. Perhaps the analogy may warrant criticism, but every surgeon knows the extent to which the sphincter can be dilated without disaster. We have followed those patients who have

external drainage is desired. This type of tube, however, does offer considerable resistance to removal and doubtless produces some trauma to the duct. In routine cases we have found a No. 10 or 12 French whistle-tipped catheter entirely satisfactory. It should be of live rubber and the suture passing through it should not weaken the tube enough for it to break at the time of removal nor should the suture pass entirely through its lumen. In small ducts it is well to point the end of the tube toward the liver. In large ducts its direction is of less importance, but there are some advantages in pointing it toward the duodenum, chiefly because this direction may cause less collection of debris in the current of bile and thereby enhances the passage of an overlooked stone. Whatever type of tube one uses, it is imperative to ascertain that bile is flowing freely through it before closing the abdomen. If this precaution is followed, there will be few cases of bile peritonitis following duct exploration. If, by chance, one finds at the end of a few hours that no bile is coming from the tube but that the dressings are saturated, then one must assume that bile peritonitis will result. If little or no bile is coming from either tube or drain at the end of twenty-four hours, the resultant discomfort, restlessness, and rapid pulse in such a patient will indicate bile peritonitis. The mortality from such a complication is high, approximately 25 per cent, while those who survive have a stormy convalescence. Although it is difficult for a surgeon to admit that there is a mechanical fault in his technique, under these circumstances he should correct this error at the earliest possible moment. By a rearrangement of the drainage in the early hours after operation, a fatality may be prevented and in every instance an easier convalescence obtained. If one waits until the manifestations of full-blown bile peritonitis have developed, the risk of secondary operations is much greater; after forty-eight hours the risk of operation usually outweighs its rewards. Bile collects above the liver in considerable quantities and this in itself creates a difficult problem and from its pressure on the diaphragm, may have some influence on the end result.

It is well to establish drainage of the most dependent part of this region of the abdominal cavity by cigarette wick or soft rubber tube, regardless of whether or not the common duct has been explored, although by taking great pains one may feel secure in many instances in not leaving a wick through the abdominal wall. Doubtless, long series of successful operations on the biliary system without drainage can be reported. Once in a great while, however, one is greatly comforted by the presence of such a tube. An accessory duct may have been overlooked and may produce enough bile drainage to create a serious problem. In spite of great care an occasional tie will slip off the cystic duct. Rarely, there is late bleeding of a quantity difficult for nature to absorb. When drains are properly placed through

caliber can form in the duct itself without having passed through the previously dilated papilla before they had reached a size larger than the diameter of the outlet. Long respites from symptoms between operations indicate that these stones, as such, were not overlooked at the previous operation. Remaining fragments in the cystic duct, pancreas, or wall of the duct to act as a nucleus, sluggish bile currents, and duct diverticula are some of the possibilities that occur to us. It seems unlikely that dilatation of the sphincter within its physiologic limits could be expected to result in a permanent increase in its diameter. It is important, however, to observe the small percentage of such patients having future symptoms, and also, the fact that there has not been a single instance of any evidence of cicatricial constriction of the duct outlet following the method. Doubtless, one could cause sufficient trauma to this area to result in serious scar formation even if the instrumentation was done from within the duct. It is evident that such trauma could be accomplished more effectively if the instrumentation was made in reverse fashion through an opening in the duodenum. Deductions from animal experiments along this line are difficult to evaluate since one cannot reproduce the various pathologic processes found in the human biliary system.

Drainage of an explored duct is wise in all instances, since a safety valve of this nature aids in the control of liver decompression; it also gives some information regarding the character and quantity of the bile secreted. The best reason for drainage, however, is based on the difficulty of accurate closure of the incision in the average duct without narrowing it. In very large ducts one may feel more secure about effecting a water-tight suture line and, occasionally, in such a case omission of the tube might be justified. When stones are known to remain in the hepatic ducts, it seems desirable to avail oneself of any effect from hydrostatic pressure within the biliary system. With a dilated papilla in a large duct, this may not be influenced by closure of the incision to any great extent; still, it eliminates the tube which may prevent stones from passing by it. After dilatation of the duct outlet, one does not need prolonged external drainage since the bile will flow freely into the duodenum in all cases as soon as any reactionary edema from the manipulation has subsided. It was found that external drainage ceased almost at once when the tube was removed at the end of ten days in our patients who had had dilatation of the papilla. When the papilla was not dilated, prolonged external drainage of bile occurred after removal of the tube in many cases.

It probably matters very little what type of tube is used to drain the common duct. Many surgeons still prefer the routine use of the T-tube and this is a satisfactory method. It should always be used after reconstruction operations upon the duct and when prolonged

external drainage is desired. This type of tube, however, does offer considerable resistance to removal and doubtless produces some trauma to the duct. In routine cases we have found a No. 10 or 12 French whistle-tipped catheter entirely satisfactory. It should be of live rubber and the suture passing through it should not weaken the tube enough for it to break at the time of removal nor should the suture pass entirely through its lumen. In small ducts it is well to point the end of the tube toward the liver. In large ducts its direction is of less importance, but there are some advantages in pointing it toward the duodenum, chiefly because this direction may cause less collection of debris in the current of bile and thereby enhances the passage of an overlooked stone. Whatever type of tube one uses, it is imperative to ascertain that bile is flowing freely through it before closing the abdomen. If this precaution is followed, there will be few cases of bile peritonitis following duct exploration. If, by chance, one finds at the end of a few hours that no bile is coming from the tube but that the dressings are saturated, then one must assume that bile peritonitis will result. If little or no bile is coming from either tube or drain at the end of twenty-four hours, the resultant discomfort, restlessness, and rapid pulse in such a patient will indicate bile peritonitis. The mortality from such a complication is high, approximately 25 per cent, while those who survive have a stormy convalescence. Although it is difficult for a surgeon to admit that there is a mechanical fault in his technique, under these circumstances he should correct this error at the earliest possible moment. By a rearrangement of the drainage in the early hours after operation, a fatality may be prevented and in every instance an easier convalescence obtained. If one waits until the manifestations of full-blown bile peritonitis have developed, the risk of secondary operations is much greater; after forty-eight hours the risk of operation usually outweighs its rewards. Bile collects above the liver in considerable quantities and this in itself creates a difficult problem and from its pressure on the diaphragm, may have some influence on the end result.

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a small stab wound, the original incision is not influenced by a foreign body. This is further obviated by the transverse incision, in which case the outer end of the wound may allow for drainage in an ideal manner. Drainage should be established to the subhepatic space described by Morison¹¹ since this is the most dependent area in the right upper quadrant. If one uses a longitudinal incision or any of its modifications and attempts to establish drainage from this deep pocket through the incisional wound, the drain must be very long. The drains have a tendency to be lifted out of the ideal position if any distention of the abdomen takes place after operation. Such foreign bodies passing through the incision are conducive to wound infection and subsequent hernia in scar. If one adopts the method of a short wick directly to the area by which all drainage from the biliary tract area must pass or collect, great care must be taken that the counter incision is accurately made. The wicks must be placed under vision and not by touch alone. It is best not to use such a method in obese individuals and usually not in secondary operations. In the former, this tunnel through the fat may be too narrow to allow for the adequate escape of material along its course. In the latter, adhesions between the liver and parietal peritoneum or to the hepatic flexure of the colon may interfere with the establishment of ideal drainage since the subhepatic space itself may be obliterated. In the average patient, however, one finds the convalescence materially shortened by the accurate establishment of a short drain through the abdominal wall directly into this subhepatic pocket. This eliminates wound contamination and creates little disturbance on removal. It doubtless causes fewer adhesions in the region of the operative field and further reduces the chances of duodenal irritation. In our cases there has been no evidence that stab wound drainage increases the risk of bile peritonitis or subdiaphragmatic abscess.

SUMMARY AND CONCLUSIONS

1. A simple and satisfactory method of cholecystectomy from the fundus toward the ducts is presented. The safety of this method is stressed.

2. Exploration of the common hepatic duct should be carried out in conjunction with cholecystectomy in a high percentage of cases. The indications for duct exploration should be carefully determined in each instance.

3. Routine dilatation of the papilla of Vater in common duct exploration is advocated. The morbidity is lowered and secondary operations are rarely necessary when this procedure is carried out.

4. If the duct is opened, it should usually be drained by a suitable tube.

5. The region of the operative field should be drained after nearly all operations upon the biliary system.

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THE PROTECTION OF THE LIVER FROM INJURY

I. S. RAVDIN, B.S., M.D., PHILADELPHIA, PA.

(From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Surgical Clinic of the Hospital of the University of Pennsylvania)

IT WAS not long after the demonstration by Simpson of chloroform as an anesthetic agent that it was found that necrosis of the liver at times followed its use.¹ The work and concepts of Rosenfeld² led to the suggestion that the administration of glucose might be of value not only in the prevention, but also in the treatment of hepatic necrosis induced by chloroform anesthesia. Rosenfeld² stated, in fact, that the detoxifying power of the liver (*entgiftenden Fähigkeiten*) is the greater the richer its content of carbohydrate.

In 1908 Wells³ offered an acceptable explanation of the greatly increased susceptibility of the fatty liver to damage by chloroform. The clinical observation that chloroform particularly affected fatty livers when added to the well-known solubility of chloroform in fats led Wells to state: "It would seem probable, therefore, that a fatty liver would abstract much more chloroform from the blood than a normal liver, and that this chloroform would thus act more strongly and for a longer time on the protoplasm of the fatty liver cells than it would in a normal liver."

That a diet high in carbohydrate is protective and that a diet high in fat induces maximal susceptibility of the hepatic parenchyma when the liver is exposed to chloroform has been repeatedly confirmed since first reported in this country by Opie and Alford.⁴ Diets rich in protein have also been found to be of value in protecting the liver against such injury, although their exact value has not been uniformly agreed upon. Starvation also markedly increases the susceptibility of hepatic parenchyma to injury by chloroform and various fat-soluble agents.

These experimental studies and their confirmation by Davis, Hall, and Whipple,⁵ Graham,⁶ and others led surgeons to believe that a high concentration of hepatic glycogen in itself would protect the liver from injury during operation and anesthesia, and furthermore that a high carbohydrate dietary was the most satisfactory means, subsequent to operation, of providing conditions conducive to hepatic cellular repair.

Davis, Hall, and Whipple⁵ had reported that under the favorable circumstances of a high carbohydrate diet the liver could regenerate itself at the rate of nearly 100 Gm. of liver tissue a day. They also showed that the urinary nitrogen excretion was greatly increased following chloroform anesthesia and that, while this was accentuated in the

fasting animal, it was greatly decreased when glucose was administered during the postanesthetic period.

It was not long before emphasis on the intravenous injection of glucose as a pre- and postoperative measure in poor surgical risks presenting lesions of the biliary apparatus replaced emphasis on a high carbohydrate dietary. Eleven years ago I stated: "In many clinics the administration of dextrose is merely a routine procedure and little thought is given to the objects to be attained by its use. . . . If glycogen can be deposited, can this be done more readily by the intravenous injection of dextrose or can it be as easily attained by the ingestion of a high carbohydrate diet?"

The rich carbohydrate diet which we used in the experiments reported eleven years ago contained approximately 80 per cent of carbohydrate and 20 per cent of protein. We were led to conclude that: "The liver cells regenerate rapidly on a high carbohydrate diet. They will not regenerate to the same extent on a diet low in carbohydrate."

TABLE I

| DIET | CONTROL | | EXPERIMENTAL APPORTIONMENT OF LIVER DAMAGE | | |
|---|---|--|---|-----------------|-------------------------|
| | AVERAGE LIVER GLYCOGEN (GM. %) | AVERAGE LIVER FATTY ACIDS (GM. %) | DEGENER- ATION (%) | NECROSIS (%) | TOTAL DAMAGED (%) |
| <i>Liver Damage at Ascending Fat Levels*</i> | | | | | |
| Low fat | 4.9 | 10.5 | 13 | 8 | 21 |
| Medium fat | 4.5 | 24.1 | 29 | 63 | 92 |
| High fat | 3.7 | 49.7 | 3 | 97 | 100 |
| <i>Liver Damage at High and Low Glycogen Levels</i> | | | | | |
| High glycogen | 6.2 | 18.4 | 13 | 49 | 62 |
| Low glycogen | 2.0 | 19.3 | 40 | 31 | 71 |

*Thirty or more rats in each group.

Evidence which Goldschmidt, Vars, and I have recently published⁸ has led us to conclude that the incidence and severity of the damage to hepatic cells, following chloroform anesthesia, increase progressively with an increase in the concentration of lipid in the liver (Table I). Regardless of the concentration of glycogen in the liver at the time of anesthetization, the findings demonstrate that increasing lipid concentrations of the liver increase its susceptibility to chloroform. While the concentration of glycogen per se had no influence in modifying the incidence or the severity of the injury, this could be modified by the protein content of the ration fed for some days prior to anesthetization for the incidence of necrosis was but 50 per cent as high when a high protein diet was given (Table II). To recapitulate, a high concentration of hepatic glycogen per se failed to confer any discernible protection against the hepatotoxic action of chloroform in rats with the same concentration of hepatic lipid and a similar intake of protein in the diet.

These data, striking as they are, force us to modify our concept of the mechanism by which carbohydrate may provide protection against certain hepatotoxic agents and have led to further investigations, the results of which are of considerable importance in this field of therapy.

We were led to conclude, after reviewing the evidence, that the chief reason for the protection against hepatic injury following a high carbohydrate diet is probably the reduction in the lipid content of the liver which results from such a diet. Furthermore, under certain conditions, such as inanition, the administration of carbohydrate probably also protects the liver by virtue of its protein-sparing action. Thus the protective action of carbohydrate is purely an indirect one.

TABLE II
LIVER DAMAGE ON HIGH AND LOW PROTEIN DIETS (RATS)

| DIET | CONTROL | | EXPERIMENTAL APPORTIONMENT OF LIVER DAMAGE | | |
|--------------|---|--|---|-----------------|-------------------------|
| | AVERAGE LIVER GLYCOGEN (GM. %) | AVERAGE LIVER FATTY ACIDS (GM. %) | DEGENER- ATION (%) | NECROSIS (%) | TOTAL DAMAGED (%) |
| High protein | 1.9 | 22.3 | 43 | 41 | 84 |
| Low protein | 6.9 | 23.5 | 6 | 88 | 94 |

In contrast to this, a diet containing an adequate amount of protein (17 per cent of the total calories) was found markedly to reduce the incidence and degree of hepatic necrosis, even in livers with a high lipid content. Less than one-half the animals on a high protein intake had liver necrosis (Table II). The protective action of protein in these experiments was not associated with the marked lipotropic action of protein which has been shown by Channon and Wilkinson,⁹ for comparisons were made in animals with similar hepatic lipid concentrations. Thus, an adequate amount of protein in the dietary would appear to protect the liver both as the result of some intrinsic property of the protein itself and because the administration of an adequate amount of protein leads to a reduction in the content of hepatic lipid.

The increased susceptibility of the liver of the starved animal, we believe, is principally due to its depleted protein stores. The question of protein storage in the body, following the administration of a diet high in protein, is of particular importance if we assume that the protection conferred by such a diet is due to the protein per se. Whether the protein is stored in the sense that carbohydrate and fat are stored in the liver, or whether it is elaborated into hepatic or other tissue, it serves to protect the cells or replenish a structure which is being attacked.

Regardless of whether or not Whipple's concept¹⁰ of "labile protein stores" proves finally to be acceptable, it is of interest that investigators in the field of protein storage have invariably directed their efforts

to the liver as the most probable repository for protein. Luck¹¹ has found that the total protein content of the liver, as well as the amount per unit of weight, is increased in those animals fed a high protein diet over those fed a low protein diet. Addis, Poo, and Lew,¹² in a study of the loss of protein from various tissues during a fast, found that the liver loses much more of its original protein content than any other organ. This fact "suggested that it [the liver] may be a depot for stored protein and that this special sort of protein may be used during fasting in much the same manner as glycogen is used during a fast."

From our own data and the support obtained from investigators in somewhat related fields, we have concluded that a liver high in lipid content and low in readily available protein is maximally susceptible to chloroform; while a liver low in lipid content and high in readily available protein is maximally resistant to injury by this agent.

The problem that confronts us is how best to induce conditions in the liver favorable to resistance to hepatotoxic agents on the one hand and to facilitate repair on the other. Such a liver should be low in lipid content and contain adequate amounts of protein.

Johnson, Vars, Zintel, and I¹³ have shown that this condition is best brought about, in dogs, with common duct obstruction and cholecystectomy by a diet consisting of approximately 28 per cent of protein and 72 per cent of carbohydrate. These later experiments have illustrated the fact that not only is a diet of suitable composition of importance but it is equally important that the total calorie intake be adequate (Table III).

With a similar total calorie intake in both the high carbohydrate-low protein and the high carbohydrate-high protein diets the lipid concentration of the liver is reduced similar amounts in half the time when adequate protein is ingested. Furthermore, with such a diet the glycogen deposition in the liver reaches the highest levels obtained in our experiments.

The presence of a high protein content in the diet makes it possible for considerable amounts of fat to be ingested and still reduce the original lipid concentration in the liver. These experiments again and again point out the fact that diet and total calorie intake are important, for one without the other will not bring about the desired effects. In view of these data it seems hardly possible that we shall continue to place emphasis on the intravenous injection of glucose. Under the most favorable conditions of such therapy one can hardly provide more than 1,200 calories per day and this cannot be continued over long periods.

If the objects we wish to attain are to be achieved, they cannot be accomplished by providing but two-thirds of the calories necessary for basal energy requirements. A suitable program requires alimentary feeding, for only in this way can one provide for the basal requirements

TABLE III
EFFECT OF DIET ON LIVER FAT IN PRESENCE OF COMMON DUCT OBSTRUCTION

| DIET | WEIGHT | | | DAYS ON DIET | CALORIES | | | LIVER GLYCOGEN | | LIVER FATTY ACID | |
|------------------------------------|---------|-----------|----------|--------------|-----------------|-------------|----------------------|------------------|-------------------|------------------|----------------|
| | INITIAL | OPERATIVE | TERMINAL | | PROTEIN (GM. %) | FAT (GM. %) | CARBOHYDRATE (GM. %) | CALORIES KG./DAY | OPERATIVE (GM. %) | TERMINAL (GM. %) | CHANGE (GM. %) |
| High protein carbohydrate (7 dogs) | 7.2 | 8.9 | 8.8 | 7 | 28 | 0 | 72 | 90 | 2.1 | 8.9 | 14.1 |
| High carbohydrate (4 dogs) | 7.2 | 7.5 | 6.3 | 14 | 8 | 12 | 80 | 89 | 2.2 | 5.4 | 15.5 |
| | | | | | | | | | 29.2 | | -54 |
| | | | | | | | | | 30.9 | | -48 |

and an additional amount of carbohydrate and protein for storage. While intravenously injected glucose may be used to reinforce oral feeding, it cannot now completely replace it. The glucose administered intravenously will protect the patient's stores of foodstuffs to the extent of 600 to 1,200 calories per day, depending upon whether a 5 or a 10 per cent solution of glucose is injected. Such therapy, however, will not lead to a marked prolonged deposition of glycogen in the liver for, even though it is temporarily deposited, it will be rapidly utilized for the energy requirements of the patient. Several years ago we examined histologically sections of the liver removed at operation under spinal anesthesia from patients who had received a 5 per cent glucose solution intravenously for a number of days prior to the operation. In those patients who received no food by mouth during the period of intravenous therapy the glycogen in the liver was always low and approximately one-third of the patients had large accumulations of hepatic lipid.

We have recently begun to reinvestigate more thoroughly the relationship between intravenous glucose administration and diet and liver composition in man. We have again been surprised at the frequency with which by analytical methods we have found high concentrations of lipid and low concentrations of glycogen in patients with biliary tract disease in whom during the preoperative period only intravenous therapy was administered. Only when a diet of adequate composition is given in sufficient calories can the liver of man be conditioned to minimal injury.

It is highly likely that many of the untoward reactions suffered by biliary tract patients after anesthesia and operation are due to varying degrees of degeneration or necrosis. If the lesion is of minor extent (Fig. 1), recovery can take place under favorable conditions, but when it is extensive death is inevitable (Fig. 2).

Bollman and Mann¹⁴ have reported that the addition of considerable amounts of meat extract or of meat itself to dogs with experimental cirrhosis or long-standing obstructive jaundice results in the development of abdominal ascites. We have not found that the addition of protein, chiefly in the form of casein, but also partly as meat, resulted in the occurrence of ascites more frequently than when the casein was omitted from the diet. Messinger and Hawkins¹⁵ have recently reported that they observed no untoward effects from the feeding of a meat diet to their dogs, even though they had severe liver injury.

From the results of our experiments, we believe that a high carbohydrate-high protein dietary will prove to be more efficacious in conditioning the liver to minimal injury than will a haphazard diet, a diet consisting of high carbohydrate-low protein, or the intravenous administration of glucose with little emphasis on the oral intake of food.

Soskin¹⁶ has recently advanced arguments in favor of the intravenous administration of glucose where hepatic glycogen deposition is desired.

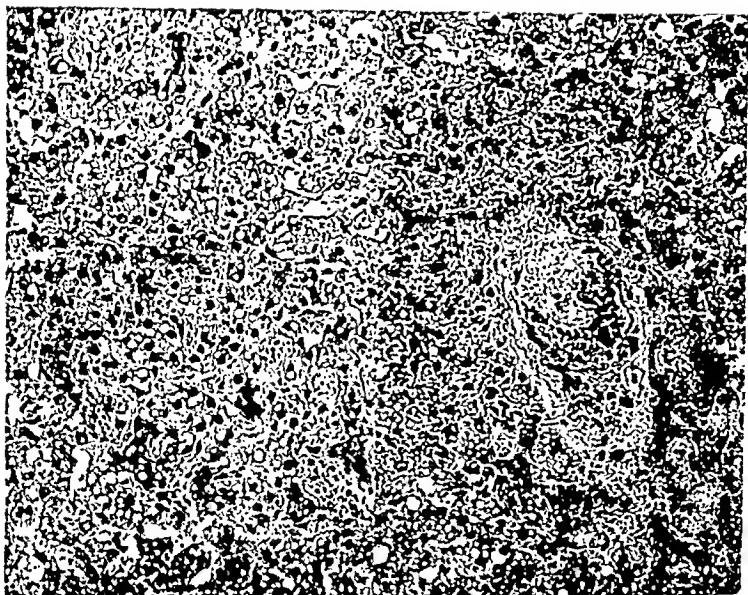


Fig. 1.—Minor necrosis of the liver following the use of ether anesthesia.

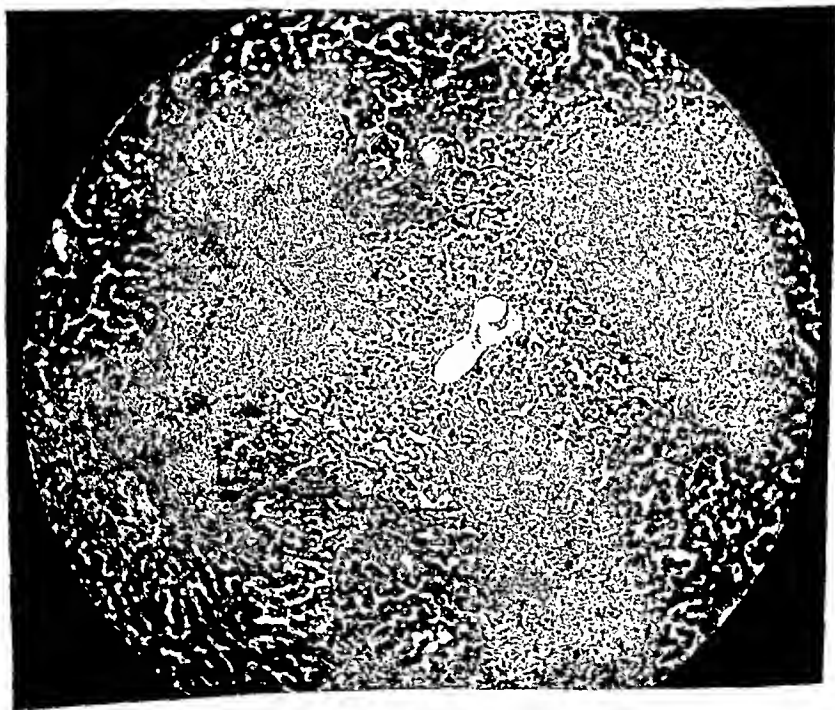


Fig. 2.—Extensive necrosis of the liver following anoxia.

Unless it becomes possible to introduce sufficient calories by this method alone or in conjunction with accessory methods of feeding the argument is without point for it is not possible to maintain the desired composition of the liver under conditions of undernutrition. The experiments we are now doing in man demonstrate that, unless an adequate caloric intake is maintained for some time prior to spinal anesthesia, glycogen deposition in man is not normal and hepatic lipid is not influenced. The amount of protein required for protection is not as yet known.

The diet, therefore, should not only be satisfactory from the standpoint of its composition, but it should be administered in sufficient amounts to insure an adequate caloric intake. The two factors can be looked upon as acting synergistically. It is not possible to outline the diet, for this must be done after consultation between dietitian and patient. It should consist of approximately 70 per cent carbohydrate, 25 per cent of protein, and not more than 5 per cent of fat in its caloric composition. From 2,500 to 3,500 calories should be given for several days prior to operation and resumed as soon as possible thereafter. If necessary the orocejunal method of feeding may be carried out. Since the oral route is at this time the only one by which a satisfactory diet of adequate caloric intake can be given it must remain the method of choice for the present. Only in those instances where oral feeding is not possible should parenteral feeding be depended upon.

Miller and Whipple¹⁷ and Messinger and Hawkins¹⁵ have confirmed our findings on the protective action of protein and the latter voice our sentiments when they state: "We suggest that in the face of liver injury a diet of protein and carbohydrate may prove to be of more value than carbohydrate alone."

Only with such a program in the pre- and postoperative periods can additional injury be prevented, or minimized, following anesthesia and operation and repair be facilitated during the period of recovery.

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THE INDICATIONS AND RESULTS OF PANCREATECTOMY FOR HYPOGLYCEMIA

VERNON C. DAVID, M.D., CHICAGO, ILL.

(From the Department of Surgery, Rush Medical College)

AFTER the discovery of insulin by Banting and Best¹ in 1922 and the later recognized effects of overdosage, Harris² in 1924 suggested a syndrome due to excessive secretion and action of insulin. Three years later Wilder and his associates³ reported the first case of hyperinsulinism and hypoglycemia due to a carcinoma of the islet tissue of the pancreas operated upon by W. J. Mayo. Since that time worldwide interest has been excited in the varying clinical picture, the pathogenesis, and the treatment of spontaneous hypoglycemia. As a result it has been established that islet-cell tumor of the pancreas gives a characteristic triad of symptoms (Whipple):^{4, 5} (1) attacks of nervous or gastrointestinal disturbances coming on in a fasting state associated with (2) a hypoglycemia with readings below 50 mg. per cent and (3) relieved immediately by ingestion of glucose. Unfortunately, the problem is complicated by the knowledge of the effect of the liver,⁶ adrenals,⁷ anterior lobe of the hypophysis,⁸ thyroid, sympathetic nervous system,⁹ and possibly other factors,^{10, 11} on sugar metabolism and particularly their effect on the development of hypoglycemia. It is, therefore, obvious that before a surgical exploration of the pancreas is decided upon not only the symptom complex of hypoglycemia indicated by Whipple must be present but also lesions of the various ductless glands mentioned must be excluded by every possible chemical, physical, and therapeutic measure. The borderline cases should be treated conservatively, care being taken not to produce great adiposity by high sugar diet. The use of anterior lobe extracts of the hypophysis has not been encouraging to date.

As a result of careful selection of cases, Whipple¹² recently reported his own series of 19 tumors of islet tissue operatively removed from

TABLE I
PARTIAL RESECTION OF PANCREAS (TUMOR FOUND)

| | NO. CASES | CURED | NO IMPROVEMENT | DIED |
|-----------|--------------|-------|-------------------|------|
| Adenoma | 11* | 8 | 1† | 2 |
| Carcinoma | 4 | 2‡ | | 2 |
| Hamartoma | 1 | 1 | | |
| | 16 | 11 | 1 | 4 |

*One patient had central nervous system damage.

†Patient had recurrent attacks after six months.

‡One patient well after four months; the other, after two months.

17 patients, and at the same time collected 65 other cases from the literature. Of these 82 cases, 65 had an islet-cell adenoma, 2 an atypical tumor, and 15 a carcinoma. There was an operative mortality of 13 patients, or 16 per cent. Of the 69 patients surviving the operation, 62 were cured of their hypoglycemia attacks and, of these, 36 had been followed for more than a year. This is truly an impressive report and would practically close the chapter were it not for the fact that a considerable number of patients have been operated upon with proper indications where no tumor of the pancreas has been found. This contingency has been considered by Whipple, who reported a group of 47 patients who had been explored (11) or whose pancreas had been more or less removed (36). Of these patients, 10 were cured, 7 improved, and 17 died postoperatively or later. A tumor was found at autopsy in 4, in the resected pancreas in 4, and at a second operation in 6. This would strongly imply that it is exceedingly hazardous to assume with careful selection of patients with hypoglycemia that a tumor of the islet cells is *not* present. This is sound reasoning as evidenced by 4 of Whipple's cases and 1 of Roseoe Graham's who had had resection of a portion of the pancreas without relief of symptoms and who at subsequent operations were found to have an adenoma of the islet cells in the head of the pancreas. Whipple also mentions 14 tumors of the pancreas overlooked at the first operation, 9 of which were found at a second operation and 5 at autopsy. Of these overlooked tumors, 7 were in the head, 5 in the tail, and 2 in the body of the pancreas.

This striking evidence for the probable presence of an islet tumor to explain spontaneous hypoglycemia of the type under discussion emphasizes the burden placed on the surgeon who not only must explore the body and tail of the pancreas but also should mobilize the duodenum, rotate it medially, and carefully examine the head of the pancreas before deciding that no tumor is present. Not all of these criteria of exploration have been carried out in the cases about to be discussed, but there have been reported a number of instances where, exploration of the pancreas failing to reveal a tumor, the surgeon has then decided upon a partial or subtotal removal of the pancreas with the hope that (1) a tumor might be found in the resected portion, (2) a hyperplasia of the islet cells might exist, or (3) removal of a considerable part of the pancreas, especially the tail and body, would cut down the insulin-secreting power of the organ.

In considering these collected cases of resection of the pancreas for hypoglycemia, the principal object has been to determine what course the surgeon has pursued when careful exploration of the pancreas failed to reveal a tumor of the pancreas and to attempt to lay down a principle of procedure based on the rather scanty literature on the subject. The cases coming under this classification would include: (1) partial resection of the pancreas, tumor found (14 cases); (2) subtotal resection of the pancreas, tumor found (3 cases); (3) subtotal resection of

TABLE II
PARTIAL RESECTION OF PANCREAS (TUMOR FOUND)

| AUTHOR | PUBLICATION | AGE | DURATION SYMPTOMS | TYPE OF SYMPTOMS | MINIMUM BLOOD SUGAR | OPERATION | PATHOLOGY | RESULT |
|--|---|-----|----------------------|-----------------------------------|---------------------------|---|----------------------------|---|
| 1. J. S. Tomkies | Texas State J. Med. 26: 523, 1932. | 30 | 3 yr. | Unconsciousness | 41 | Part of body and part of tail | Encapsulated adenoma | Symptom free 6 yr. |
| 2. C. L. Derick et al. | New England J. Med. 268: 243, 1933. | 56 | 6 yr. | Coma | 38 | Tail resected | Adenoma in tail | Symptom free 5 yr. |
| 3. E. A. Graham and N. A. Womaek | Surg. Gynce. & Obst. 56, 728, 1933. | 22 | 5 yr. | Petit mal con- fusion | 25 | 4 cm. tail re- sected; nod- ule excised | Adenoma | No attacks; central nerv- ous system damaged |
| 4. A. O. Whipple (Case 5) | Ann. Surg. 101: 1299, 1935. | 28 | 6 yr. | Unconsciousness | 28 | Resection tail and part of body | 2 adenomas | Symptom free 3 yr. 1 mo. |
| 5. G. E. Cheley | Tr. West. S. A. 44: 98, 1934. | 50 | 13 yr. | Unconsciousness | 30 | Partial resec- tion | Adenoma | Symptom free 3½ yr. ex- cept for ex- haustion and amnesia |
| 6. O. Wangen- steen (Case 1) | Minnesota Med. 18: 265, 1935. | 28 | 3 yr. | Convulsions, un- consciousness | 15.5 | Resection tail | Adenoma | Symptom free 3 yr. 4 mo. |
| 7. M. Munakata | Arch. f. klin Chir. 185: 624-632, 1936. | 40 | 14 mo. | Coma | 33 | Partial resec- tion | Carcinoma epi- thelioma | Symptom free 4 mo. |

| S. E. J. Kepher and W. Walters | Proc. Staff Meet. Mayo Clin. 11: 454, 1936. | 46 | 2 yr. | Convulsions | 35 | Partial resection | Adenoma | Symptom free 2 yr. 4 mo. |
|--|--|----|--------|--------------------|-----|---|-----------------------------|---|
| 9. E. Zickind and W. A. Bailey | J. Lab. & Clin. Med. 23: 231, 1937. | 38 | 2 yr. | Convulsions, mania | 44 | Exploration; no tumor; partial resection | 2 adenomas | Died 32 hr. postoperatively |
| 10. P. S. Federoff (Case 2) | Urach. gaz. 35: 585-592, 1931. | 16 | | | Low | Partial resection | Carcinoma | Died |
| 11. A. O. Whipple (Case 8) | Internat. S. J. 3: 1, 1938. | 51 | 1 yr. | Unconsciousness | 54 | Partial resection | Adenocarcinoma islet tissue | Died fifth day |
| 12. M. Isaji | Frankfurt. Ztschr. f. Path. 53: 178-207, 1939. | 63 | | Unconsciousness | 41 | Partial resection 16 Gm. with tumor | Adenoma | Died second day |
| 13. A. O. Whipple (Case 9) | J. Internat. Chir. 3: 1, 1938. | 45 | 8 mo. | Unconsciousness | 26 | Partial resection; excision | 2 adenomas | Improved 2 mo. |
| 14. A. O. Whipple (Case 10) | J. Internat. Chir. 3: 1, 1938. | 50 | 6 mo. | Convulsions | 27 | Partial resection | Carcinoma of islet tissue | Improved 2 mo. |
| 15. T. Bailey and E. C. Cutler | J. Internat. Chir. 3: 1, 1938. | 56 | 17 mo. | Unconsciousness | 31 | Tail and part of body (14.5 Gm.) | Hamartoma | 10 mo. no attacks |
| 16. J. M. McCaughan and G. O. Brown (Case 4) | Ann. Surg. 105: 354, 1937. | 27 | | Convulsions | 52 | 23 Gm. tail and body; exploration 2 mo. later | Islet adenoma tail | Improvement 6 mo.; recurrence of symptoms 6 mo. postoperatively |

TABLE III
PARTIAL RESECTION (NO TUMOR) NORMAL PANCREAS OR HYPERPLASIA

| AUTHOR | PUBLICATION | AGE | DURATION SYMPTOMS | TYPE OF SYMPTOMS | MINIMUM BLOOD SUGAR | OPERATION | PATHOLOGY | RESULT |
|---|-------------------------------------|-----|-------------------|-------------------|---------------------|--|-----------------------|--|
| 1. J. M. T. Finney and J. M. T. Finney, Jr. | Tr. Am. S. A. 46: 268, 1928. | 53 | 4 yr. | Unconsciousness | 30 | Resected 22.05 Gm. | Normal pancreas | Attacks continued |
| 2. F. N. Allan et al. | J. A. M. A. 94: 1116, 1930. | 52 | 2 yr. | Stupor | 40 | Resection 14 Gm. tail and part body | Normal pancreas | No improvement |
| 3. F. N. Allan et al. | J. A. M. A. 94: 1116, 1930. | 47 | 4 yr. | Convulsions | 40 | 8 Gm. excised | Normal pancreas | No improvement |
| 4. F. N. Allan et al. | J. A. M. A. 101: 99, 1933. | 42 | 1 yr. | Coma | 40 | 8 Gm. tail excised | Normal pancreas | No permanent improvement |
| 5. E. Holman et al. | Surg. Gynec. & Obst. 56: 591, 1933. | 31 | 2 yr. | Convulsions, coma | 32 | Resection; number Gm. not mentioned | Normal pancreas | No improvement |
| 6. J. A. Evans and W. McDonough | J. Iowa M. Soc. 23: 454, 1933. | 41 | 1 yr. | Spells | ? | Resection | Normal pancreas | No improvement |
| 7. R. D. Forbes et al. | West. J. Surg. 47: 76, 1939. | 59 | | Unconsciousness | Low | 9.5 Gm. tail | Hyperplasia (?) tumor | Blood sugar back to normal |
| 8. H. Reid | Tr. West. S. A. 44: 97, 1934. | 22 | 8 yr. | Convulsions | 60 | Partial resection | Normal pancreas | Well except for slight attacks 4 yr. postoperatively |
| 9. O. Wangersten (Case 4) | Minnesota Med. 18: 520-566, 1937. | 29 | 9 mo. | Unconsciousness | 46 | (1) Excised tail; (2) exploration; (3) partial resection | Normal pancreas | Died sixth post-operative day |

| 10. A. J. Berry | Brit. J. Surg. 33: 51, 1935. | 38 | 14 yr. | Convulsions | 45 | Partial resection 28 Gm. | Normal pancreas | Improved |
|--|--|----|--------|---------------------------|----|---------------------------------|-----------------|---|
| 11. L. Goerry and G. T. McCutchen | Ann. Surg. 104: 602, 1936. | 45 | 3 yr. | Convulsions | 30 | Resection | Normal pancreas | Died on operating table |
| 12. O. Vangenstein (Case 5) | Minnesota Med. 20: 566, 1937. | 2½ | 2 yr. | Convulsions | 23 | Partial resection | Normal pancreas | Normal blood sugar; died 6 wk.; infection |
| 13. A. F. Hartman and J. C. Jaudon (Case 18) | J. Pediat. 11: 1, 1937. | 1 | 9 mo. | Convulsions | 6 | Partial resection | Normal | Symptom free 4 yr.; mentally backward |
| 14. J. A. Barnes and E. L. Richmond | New England J. Med. 213: 225, 928, 1935. | | | Unconsciousness, rigidity | 30 | Partial resection 2 inches tail | Normal pancreas | Died 3 days; pneumonia; no tumor found at autopsy |
| 15. A. O. Whipple | J. Internat. Chir. 3: 1, 1938. | 25 | 6 mo. | Drowsy | 35 | Partial resection | Normal | Symptom free 1 yr. 9 mo. |
| 16. J. McCaughan and G. O. Brown (Case 5) | Ann. Surg. 105: 351, 1937. | 50 | 3 yr. | Convulsions | 62 | Partial resection 5 Gm. | Hyperplasia | Some improvement |
| 17. J. McCaughan and G. O. Brown (Case 1) | Ann. Surg. 105: 351, 1937. | 20 | 3 yr. | Convulsions | 52 | Partial resection 8 Gm. | Hyperplasia | Recurrent symptoms |
| 18. J. McCaughan and G. O. Brown (Case 2) | Ann. Surg. 105: 351, 1937. | 17 | 4 yr. | Convulsions | 45 | Partial resection 22.5 Gm. | Normal pancreas | Recurrent symptoms |

the pancreas, no tumor found, but subsequently found (4 cases); (4) partial resection of the pancreas, no tumor found, pancreas normal or hyperplasia of the islet tissue (19 cases); (5) subtotal resection of the pancreas, pancreas normal or hyperplasia of the islet tissue (17 cases).

It is difficult to decide arbitrarily what constitutes a partial and subtotal resection of the pancreas, many of the reports failing to state the exact number of grams of tissue removed. The size of the patient and the size of the pancreas also enter into the problem. Bailey and Cutler,¹³ in discussing this matter, suggest that, inasmuch as the normal pancreas weighs between 60 and 90 Gm., at least four-fifths of the organ should be removed to constitute a subtotal removal. This would amount to 48 to 72 Gm. Another yardstick would be the surgeon's own conception of how much of the pancreas was removed, estimating that removal of two-thirds to four-fifths of the organ would constitute subtotal removal.

If we consider Tables I and II tabulating 16 cases of partial resection of the pancreas where a tumor was found, it is evident that all of these patients had a very low fasting blood sugar and the symptoms of hypoglycemia were severe. The resection of the pancreas consisted in most part of removal of the tail or the tail and part of the body of the pancreas. The amount of pancreatic tissue removed, when stated, was up to 23 Gm. The character of the tumor found in the resected tissue was islet adenoma, 11; carcinoma, 4; hamartoma, 1. There were 4 postoperative deaths. Eleven of the remaining patients remained symptom free of attacks of hypoglycemia for from four months to six years, 7 having been observed for more than two years. One patient had a recurrence of symptoms six months postoperatively.

In 2 patients where subtotal resection of the pancreas was carried out and the tumor was found in the resected portion, 1 patient died postoperatively but the other remained symptom free for ten months.

In 4 patients a subtotal resection of the pancreas was carried out and no tumor was found in the resected specimen. Subsequently a tumor was found and removed from the head of the pancreas.

Summarizing this group of 22 patients where a partial or subtotal pancreatectomy was carried out because of hypoglycemia and a tumor was found in the resected portion or at a subsequent operation, the results are simply those that one would expect following the successful removal of an islet tumor. This group also emphasizes the importance of careful exploration of all parts of the pancreas and the advisability of resection of the pancreas if no tumor can be found. If inadvertently the head of the pancreas were not explored and resection of the gland did not result in cure, a plain indication for another operation and exploration of the head of the pancreas is present.

Our interest in this study lies in the two groups of patients having partial or subtotal removal of the pancreas for spontaneous hypogly-

TABLE IV
PARTIAL RESECTION OF PANCREAS (NO TUMOR FOUND)
(FROM 8 TO 28 GM. OF PANCREAS REMOVED)

| | NO. CASES | CURED | IMPROVED | NO IMPROVEMENT | DIED |
|-------------|--------------|-------|----------|-------------------|------|
| Normal | 15 | 2* | 2 | 7 | 4 |
| Hyperplasia | 3† | 1 | 1 | 1 | — |
| | 18 | 3 | 3 | 8 | 4 |

*One patient was a 9-month-old baby.

†Nine and one-half grams of tail removed, question of tumor.

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cemia where no tumor was found in the resected portion of the pancreas and the pancreatic tissue removed was normal or showed a hyperplasia of the islet cells.

In Table IV where a partial resection of the pancreas was carried out in 18 patients and no tumor was found, there were 15 patients in whom the pancreas was normal histologically and 3 in whom hyperplasia of the islet cells was present. The minimum blood sugar in this group was below 50 mg. per cent in 14 patients. There was an operative mortality of 4 patients, or 22 per cent. Of the 14 survivors only 3 were free from attacks, 3 were moderately improved, and in 8 patients the attacks continued. Of these patients, 4 had 14 to 28 Gm. of pancreas removed, with some improvement in 1 and no abatement of symptoms in 3.

In Table V we have listed a group of 17 patients who have had a removal of from 35 to 60 Gm. of pancreas for spontaneous hypoglycemia. No tumor was found in the resected tissue in these patients. The examination of the pancreatic tissue revealed a normal pancreas

TABLE V
SUBTOTAL RESECTION OF PANCREAS
(FROM 35 GM. TO 90% OF PANCREAS REMOVED)

| | NO. CASES | CURED | IMPROVED | NO IMPROVEMENT | DIED POST- OPERATIVELY |
|-------------------------------------|--------------|-------|----------|-------------------|---------------------------|
| <i>No Tumor Found</i> | | | | | |
| Pancreas normal | 14 | 10 | 1 | 2 | 1 |
| Hyperplasia of the islets | 2 | 1 | — | 1 | — |
| Pancreatitis | 1 | 11 | — | 1 | — |
| | 17 | 11 | 1 | 4 | 1 |
| <i>Tumor Found in Resected Area</i> | | | | | |
| | 2 | 2 | — | — | — |
| <i>No Tumor Found</i> | | | | | |
| | 4 | 3 | 1 | — | — |
| Total | 23 | 16 | 2 | 4 | 1 |

TABLE VI—CONT'D

| AUTHOR | PUBLICATION | AGE | DURATION SYMPTOMS | TYPE OF SYMPTOMS | MINIMUM BLOOD SUGAR | OPERATION | PATHOLOGY | RESULT |
|-------------------------------------|---|-----|----------------------|-------------------------|---------------------------|---|---------------------|--|
| 17. W. C. Carrol | Minnesota Med. 20: 229, 1937. | 30 | 9 mo. | Unconsciousness | 55 | Resection 54 Gm. | | Improved 1½ yr.; nervous depres- sion |
| <i>Tumor Found in Resected Area</i> | | | | | | | | |
| 1. O. Wangersen (Case 2) | Minnesota Med. 18: 265, 1935. | 37 | | Convulsions | 30 | Subtotal resec- tion ¾ to ⅔ | Adenocar- cinoma | Symptom free 3 yr.; mental de- terioration |
| 2. L. P. Engle | Personal com- munication to Whipple | 38 | | Unconsciousness | Low | Subtotal resec- tion | Adenoma in tail | Symptom free 10 mo. |
| <i>No Tumor Found</i> | | | | | | | | |
| 1. R. Graham | Personal com- munication to Whipple | 27 | | Unconsciousness | 26 | (1) Subtotal resection; (2) subse- quent re- moval ade- noma in head | Adenoma | No change symp- toms; improve- ment |
| 2.) 3.) A. Whipple 4.) | Chicago Surg. Soc. Dec., 1939. | | | Hypoglycemic attacks | Under 50 | Subtotal resec- tion subse- quently find- ing tumor in head | Islet tumors | |

in 14 patients, hyperplasia of the islet cells in 2, and a pancreatitis in 1 patient. Of these patients, 11 are relieved of the symptoms of hypoglycemia, 7 having been followed for over two years. There was only 1 operative death. Of the 4 unimproved patients, two had a fasting blood sugar of 65 to 70 mg. per cent before the operation and therefore may not strictly belong in the group giving the characteristic triad of symptoms.

There were 15 patients having a removal of 40 to 60 Gm. of pancreas where no tumor was found. Ten of these patients are apparently cured.

We have included in the group of patients cured of their attacks of hypoglycemia one patient who has subsequently shown evidence of mental deterioration (Graham's case), one patient who has had an occasional flexor spasm in one arm, and still another who has had two periods of nervous depression since the operation.

If we consider the mortality rate of the 23 patients who have had a resection of over 30 Gm. of pancreatic tissue, we find it to be 4.3 per cent. This low mortality rate compared to the 16 per cent mortality in removal of adenomas is probably a happenstance but still indicates that the operation is fairly safe.

This review of the results of partial and subtotal pancreatectomy was prompted by an experience in resection of 48 Gm. of pancreas in a patient with marked hypoglycemia where no tumor was found and the patient has remained well for nearly two years following the operation. Only a short case history will be given here as a more detailed description of the case will be given elsewhere by Rollin T. Woodyatt and Leo K. Campbell.

CASE REPORT

A male, 21 years of age, came to the Presbyterian Hospital on May 1, 1938, with no significant past history or dietary indiscretions, and developed in the course of a few days severe generalized tonic and clonic seizures with marked muscle irritability and local muscle spasm between the severe attacks. His laboratory findings were: serum Ca, 9.5; serum protein, 2; urea nitrogen, 12.7; uric acid, 3.8; creatinine, 1.3; total N.P.N., 33.3; CO₂ volume per cent, 48.7; chloride as NaCl, 479; Kahn, negative.

| | |
|--------------------------------|-----------|
| Glucose tolerance | Sugar 95 |
| 1 hour | Sugar 66 |
| 2 hours | Sugar 91 |
| 3 hours | Sugar 107 |
| The urine sugars were 35.6 mg. | |
| | 49 mg. |

The sella turcica was normal. Cortin was given in doses of 1 to 4 c.c. for five days without effect. When the patient came to the operating room, in spite of a previous injection of hypertonic glucose solution, he had a convulsion on the table so that more sugar was given and continued during the operation. The operation was carried out on May 27, 1938, under gas ether. A transverse upper abdominal incision was made. The gastrocolic omentum was divided. Careful examination

revealed no tumor in a rather small, pale pancreas. The adrenal glands were normal. Beginning at the tail, the pancreas was mobilized from below upward, but as the resection began it was found that the splenic vessels were imbedded in the superior surface of the pancreas so they were divided somewhat to the right of the median line. Forty-eight grams of pancreas were removed as well as a normal-appearing spleen. The pancreas was removed by sharp dissection, catching the vessels as they appeared. The cut surface of the pancreas was approximated with interrupted catgut stitches. A small nodule of pancreas was left in the curve of the duodenum. Two cigarette drains were left. Following the operation the patient was transfused. The day after operation the blood sugar was 280 mg. per cent and the urine showed sugar at seven drops. On June 14, 1938, the patient began to run a temperature which necessitated the opening of an abscess which was followed by a fistula which persisted about a month. The patient has been well since the operation, has had normal blood sugar and no muscular irritability.

CONCLUSIONS

In patients with the Whipple triad of symptoms and in whom extra-pancreatic causes of hypoglycemia have been excluded as carefully as possible and dietary management has failed, exploration of the pancreas is indicated. A careful search for an islet tumor including mobilization of the duodenum and inspection of the head of the pancreas failing to demonstrate a tumor, a clear indication is present for subtotal resection of the tail and body of the pancreas up to the superior mesenteric vessels. This operation has been carried out in seventeen patients whose records have been found in the literature with favorable results and should be a part of the program in the treatment of spontaneous hypoglycemia until more knowledge of the underlying causes of the condition offers a better solution of the problem.

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THE PORTAL CIRCULATION AND RESTORATION OF THE LIVER AFTER PARTIAL REMOVAL

FRANK C. MANN, M.D., ROCHESTER, MINN.

(From the Division of Experimental Medicine, the Mayo Foundation)

THE practice of surgery has undergone many progressive changes during the period of years spanned by the length of life of the two surgeons to whose memory this volume is dedicated. Not the least important of these changes has been the increased application of knowledge obtained by experimental research to clinical surgery. There also has been an increase in the utilization of surgical procedures and methods in the experimental investigation of fundamental problems relating to the patient. This paper, dealing wholly with the results of experimental research and probably without clinical significance, is presented for publication in this special volume on the basis that it is representative of one phase of surgical progress, the application of surgical methods to the experimental investigation of fundamental processes.

Many surgical procedures must be considered carefully in relation to physiologic processes because such procedures cause the loss of all or a part of a functional activity or an organ for which physiologic compensation must be made. Fortunately in most instances the body possesses a functional reserve of many organs so that the remaining organ, in the case of paired organs, or the portion of an organ can readily compensate for the physiologic loss necessarily produced by such surgical procedures. Knowledge concerning the stimulus and mechanism causing physiologic compensation for the loss of a functional activity, organ, or portion of an organ is as yet in many instances incomplete. In view of the fact that often the feasibility of an operation or the beneficial effect expected from its use depends upon certain physiologic compensations occurring as a result of its performance, studies of the causal mechanism of such compensation may be of importance.

Compensatory hypertrophy, or restoration as we prefer to name the process, occurs to a remarkable degree in the liver following injury or partial removal and is in fact one of the most outstanding characteristics of hepatic tissue. The process is readily investigated by removal of various portions of the organ which is a feasible procedure to perform in many species of animals. The results of the early investigations on the subject have been reviewed by Rous and Larimore and by Fishback.² The data obtained by these early investigators supplemented by those of several more recent studies¹⁻⁴ furnish a fairly complete history of the process of restoration of the liver after partial removal.

The restorative process appears to begin almost immediately after operation and is certainly initiated before the end of the first twenty-four hours. The rate of restoration varies, depending upon the species of animal used and the relative amount of liver tissue removed. The process occurs more rapidly and the total amount of liver tissue restored is greater when more than 50 per cent of the original liver mass is removed than when less than this amount is ablated, although it does occur even when less than 20 per cent of the hepatic tissue is removed. After the remaining liver tissue has been restored to a certain degree, no further increase occurs, even though the animal lives for many months after operation (Table I).

TABLE I
RESTORATION OF LIVER AFTER PARTIAL REMOVAL

| NO. | BODY WEIGHT AT OPERATION (KG.) | BODY WEIGHT AT NECROPSY (KG.) | TIME BETWEEN OPERATION AND NECROPSY (DAYS) | ESTIMATED WEIGHT OF LIVER AT OPERATION (3.5% BODY WEIGHT) (GM.) | AMOUNT OF LIVER TISSUE REMOVED AT OPERATION (GM.) | ESTIMATED WEIGHT OF LIVER AT NECROPSY (3.5% BODY WEIGHT) (GM.) | WEIGHT OF LIVER TISSUE AT NECROPSY (GM.) |
|-----|--------------------------------|-------------------------------|--|---|---|--|--|
| 1 | 14.0 | 13.2 | 10 | 490 | 212 | 462 | 310 |
| 2 | 11.0 | 10.0 | 11 | 385 | 220 | 350 | 270 |
| 3 | 13.2 | 12.3 | 17 | 462 | 306 | 430 | 337 |
| 4 | 14.0 | 13.3 | 57 | 490 | 278 | 465 | 460 |
| 5 | 15.9 | 14.2 | 64 | 556 | 288 | 497 | 408 |
| 6 | 11.9 | 10.2 | 98 | 416 | 340 | 357 | 418 |
| 7 | 12.0 | 10.9 | 101 | 420 | 244 | 381 | 314 |
| 8 | 10.5 | 10.2 | 133 | 367 | 212 | 357 | 310 |
| 9 | 10.1 | 11.2 | 137 | 353 | 154 | 392 | 412 |
| 10 | 11.0 | 10.5 | 306 | 385 | 245 | 367 | 326 |
| 11 | 17.3 | 16.6 | 320 | 605 | 416 | 381 | 661 |
| 12 | 15.9 | 15.6 | 321 | 556 | 256 | 546 | 414 |
| 13 | 13.3 | 13.3 | 341 | 466 | 256 | 466 | 568 |
| 14 | 11.7 | 11.9 | 347 | 409 | 281 | 416 | 570 |
| 15 | 14.5 | 14.5 | 387 | 507 | 354 | 507 | 442 |

The gross appearance of the restored liver is very characteristic and can always be readily recognized. The edges of the lobes of the restored liver are rounded as compared to the knifelike edges of the lobes of the normal organ. The body of the lobe becomes dome-shaped and the lobe as a whole tends to become spherical. Sometimes there is a prolongation of one or more lobes. There is an increased friability of the hepatic tissue and the total mass of the restored liver may increase to an amount equal to or sometimes slightly greater than the amount of tissue removed at operation.

The microscopic changes in the restored hepatic tissue are not as definite or as easily recognized as the changes in gross appearance. Immediately after operation the hepatic cells appear swollen and many

remain larger than normal for several days. Mitotic figures begin to appear very soon after operation and are most abundant during the greatest period of hepatic tissue increment. The hepatic lobules are usually larger during the restorative process. It is usually impossible to differentiate restored liver tissue from normal hepatic tissue microscopically after the completion of restoration by any known method.

There is evidence that restored hepatic tissue is in certain respects not quite the same as normal liver tissue. The restored liver appears to react slightly differently in regard to physiologic stress and hepatic poisons. However, it has never been demonstrated that it has a reduced functional capacity.

The restoration of hepatic tissue after partial removal of the organ has been given the usual terms applied to this process when occurring in other organs as compensatory or work hypertrophy and is conceived as being due to a physiologic lack. But since the liver has many functions, a deficiency of hepatic tissue should produce a physiologic lack in regard to many physiologic processes. The stimulus for restoration could be owing to overwork in respect to one or several functions. If it were proved that overwork in regard to specific functions of the liver was responsible for the restoration of hepatic tissue after partial removal, efforts could be concentrated on the investigation of methods of quantitation of one or more such functions and thus afford the possibility of development of a real functional test for the liver.

The first evidence that the restoration of the liver after partial removal might not be a work hypertrophy and the stimulus causing it a functional lack came with the discovery of methods for decreasing the restoration or abolishing it altogether.

Rous and Larimore ligated the branches of the portal vein to the main liver of the rabbit, in which species the organ is almost completely separated into two unequal parts. The portion of liver deprived of portal blood underwent simple but complete atrophy while the hepatic tissue receiving all the portal blood hypertrophied to an amount equal to the original mass of liver tissue. They found that the atrophy of the lobes with ligated portal radicles was conditioned on hypertrophy of the remaining portion. The atrophy did not occur when the hypertrophy of the other portion was prevented by occlusion of the bile ducts draining it. The results of this investigation were important in giving direction to subsequent studies.

Mann and Magath, and later Mann, Fishback, Gay, and Green⁸ removed various portions of the liver from dogs in which the portal blood had been diverted from the organ by making a stoma between the portal vein and vena cava with ligation of the former (Eck fistula) some weeks previous to the hepatectomy. They found that restoration was absent or occurred to only a slight extent in the atrophic liver deprived of portal blood. Mann and his co-workers⁹ ligated the common bile duct and

found that, after the characteristic changes in the liver due to portal obstruction had occurred, the restoration of the liver after hepatectomy was greatly decreased. They¹⁰ also found that restoration after partial removal was almost absent in the cirrhotic liver produced by the administration of carbon tetrachloride.

Stephenson¹² found that, when partial ligation of the portal vein was combined with partial removal of the liver in the rat, restoration was decreased. The amount of restoration appeared to be indirectly proportional to the amount of restriction of the portal vein.

Higgins, Mann, and Priestley⁵ studied restoration of the liver after its partial removal in the chicken. In this species as in many other species there is a natural anastomotic channel between the portal and systemic systems. The liver is divided into two main lobes, the right and left. The left lobe, which is approximately one-third of the organ, can be easily removed. Following such removal, as a rule, little, if any, restoration occurred. The anastomotic channel was then ligated and several weeks subsequently the left lobe of liver was removed. Although restoration usually occurred following these procedures, it was not marked and it was never complete. The inferior vena cava was then ligated as far cephalad as possible. This forced much of the blood from the vena cava caudal to the point of ligation through the anastomotic channel into the portal system and thus increased the flow of blood through the liver. When the left lobe of liver was removed several weeks subsequent to these procedures, restoration of the liver always occurred, was usually complete, and was often greatly in excess of the tissue removed. Furthermore, ligation of the vena cava alone was often followed by increase in size of the liver.

In many respects a liver which has lost its portal blood supply presents an exactly opposite appearance to the liver from which a portion has been removed.¹³ The hepatic tissue loses its turgidity and becomes flabby immediately after the diversion of the portal blood. The organ undergoes certain definite changes which give it a characteristic appearance. On gross examination, the most outstanding changes are in size and color. It atrophies to approximately one-half its normal size or less (Table II). Its shape and contour remain the same, but there is a decrease in all dimensions to about one-half the normal, and it becomes characteristically pale, mottled, and yellow. Microscopic changes are also definite. Atrophy of the central portions of all lobules occurs with accumulation of fat in the hepatic cells of these regions. Frequently the accumulation of fat in the hepatic cells is so great that only a rim of the protoplasm of the cell with a nucleus pushed to the periphery remains. After these changes, which occur initially in the central portion of the lobule, have extended to a considerable extent to the periportal regions, the atrophy becomes stationary and will remain thus for the remaining period of life. While Eck-fistula animals can rarely

TABLE II

ATROPHY OF LIVER AFTER DIVERTING PORTAL BLOOD (ECK FISTULA)

| NO. | BODY WEIGHT AT OPERATION (KG.) | BODY WEIGHT AT NECROPSY (KG.) | TIME BETWEEN OPERATION AND NECROPSY (DAYS) | ESTIMATED WEIGHT OF LIVER AT OPERATION (3.5% BODY WEIGHT) (GM.) | ESTIMATED WEIGHT OF LIVER AT NECROPSY (3.5% BODY WEIGHT) (GM.) | WEIGHT OF LIVER TISSUE AT NECROPSY (GM.) |
|-----|--------------------------------|-------------------------------|--|---|--|--|
| 16 | 12.2 | 10.4 | 28 | 427 | 364 | 196 |
| 17 | 14.8 | 10.6 | 35 | 518 | 371 | 168 |
| 18 | 12.4 | 10.7 | 35 | 434 | 374 | 240 |
| 19 | 15.0 | 12.8 | 35 | 525 | 448 | 268 |
| 20 | 18.5 | 15.9 | 42 | 647 | 556 | 390 |
| 21 | 14.3 | 10.7 | 42 | 500 | 374 | 180 |
| 22 | 15.5 | 12.9 | 42 | 542 | 451 | 270 |
| 23 | 21.9 | 17.3 | 42 | 766 | 605 | 350 |
| 24 | 13.4 | 9.9 | 42 | 469 | 346 | 174 |
| 25 | 19.5 | 14.9 | 49 | 682 | 521 | 250 |
| 26 | 11.9 | 9.1 | 49 | 416 | 318 | 265 |
| 27 | 14.8 | 11.8 | 56 | 518 | 413 | 240 |
| 28 | 13.9 | 11.0 | 70 | 486 | 385 | 256 |
| 29 | 11.1 | 8.8 | 70 | 388 | 308 | 164 |
| 30 | 9.2 | 7.7 | 77 | 322 | 269 | 150 |
| 31 | 11.7 | 8.1 | 84 | 409 | 283 | 156 |
| 32 | 12.1 | 8.1 | 192 | 423 | 283 | 154 |
| 33 | 18.9 | 14.3 | 192 | 661 | 500 | 234 |

be maintained at their preoperative weight, the decrease in weight of the liver far exceeds the loss in body weight.

An analysis of the various methods discovered to date which will decrease or abolish the capacity of the liver for restoration reveals the fact that in each the flow of portal blood is either restricted or completely lacking. This fact suggests that the presence of the portal circulation may be as important in the causation of hepatic hypertrophy as its absence in producing hepatic atrophy. The contrast of the rapidity and amount of restoration in a normal liver with intact portal circulation after partial removal of the organ with the almost total lack of restoration in the liver without portal blood supply is both striking and significant.

The results of the investigations cited prove that restoration of liver tissue after partial removal to a significant amount depends upon an intact portal circulation, that injuries to the liver which restrict the portal circulation also cause a decrease in restoration, and that atrophy of the liver occurs in the absence of the portal blood flow. They do not indicate whether the stimulus causing the restoration is owing to the portal blood itself or the presence or absence of some of its constituents. Since diversion of the portal blood does not decrease the need of the organism for the performance of hepatic function, it would appear that,

if the stimulus for restoration were purely functional, a liver without portal blood would also be restored. Factors which might modify this assumption are the following: The portal blood comprises approximately two-thirds of the blood supply of the liver, so that in its absence there may not be sufficient blood for restoration. Since the circulation of the liver is unique in that it comes from two sources, one of which is venous in character and carries the absorption products from the intestinal tract as well as many substances elaborated by the organs draining into it, the possibility exists that the stimulus causing restoration is in a sufficiently high concentration to act only in the portal blood. It is also conceivable that failure of restoration to occur is owing to a loss of such a capacity in the hepatic cell since all procedures which decrease restoration also injure the hepatic cell.

In order to test all these assumptions it was essential that the portion of the liver left after partial removal should have its normal supply of portal blood, be normal hepatic tissue, and not be forced to afford passage to the portal blood normally passing through the liver tissue removed. The requirements for such a test were met in part by making in the mammal an open anastomotic channel between the portal and systemic venous systems, which as previously mentioned, occurs naturally in many species of the lower forms. To accomplish this a stoma was made between the portal vein and vena cava, without permanent ligation of either, thus permitting the blood to pass freely between the two vessels, depending upon the difference in pressure in them. Various portions of the liver were then removed. If the stimulus causing restoration is due to some substance or substances in the portal blood, restoration should occur because the remaining portion of the liver was left intact with its normal circulation. If the restoration is due to the portal blood which normally passed through the liver, tissue removed being forced through the remaining portion of the liver, restoration should not occur because this excess blood could pass directly through the stoma into the vena cava. An important source of error in the method is that owing to variations in size of the stoma in relation to diameter of the portal vein, more or less blood than passed through the liver tissue removed, might be shunted into the vena cava.

METHOD

Details of the method used to test the importance of the portal circulation for restoration of the normal liver after partial removal are as follows: All experiments were performed on dogs. All operative procedures were carried out under ether anesthesia and with surgical technique. A stoma was made between the portal vein and vena cava of the same type and employing the same technique as that used in making an Eck fistula. This technique has been described elsewhere

and need not be given in detail here.² Suffice it to state that the method of establishing a common opening between the two veins consists of the following steps:

1. The operative incision extends from the costal angle at the midline to the right flank. It begins at the costal angle and is a midline incision for about 8 cm. It then cuts obliquely across the right rectus muscle to the semilunar line, along which it extends caudally as far as necessary. This incision is very important as it is the only type of incision I have found which provides adequate exposure of the proper area of the two veins.

2. The duodenum is grasped firmly and pulled upward and to the left, care being taken to prevent making a rent in the delicate mesentery of the duodenum. All of the intestines found in the right upper quadrant are packed to the left of the duodenum and its mesentery.

3. A loose linen ligature is placed around the portal vein between the site of entrance of the pancreaticoduodenal vein and the liver.

4. The adventitia is removed from the right side and anterior surface of the portal vein for a distance extending caudally as far as possible from the entrance of the pancreaticoduodenal vein. The vena cava is left undisturbed.

5. A stay suture of two strands of fine silk is placed at each end of the exposed lengths of veins, holding them tightly together at each point.

6. A continuous suture, the posterior suture line, is now placed between the two stay sutures, using the needle of the caudal stay suture.

7. A cutting suture of heavy silk on a specially curved needle is placed as a mattress suture with an arm in each vein, the base slightly caudal to the cephalic stay suture and the free ends emerging from the veins just before reaching the caudal stay suture. The needle of the cutting suture is passed into the portal vein just cephalic to the caudal end of the previously placed suture line and parallel to it. It emerges from the portal vein just before reaching the cephalic stay suture and is passed into the vena cava in the opposite direction, emerging from this vessel at a point exactly opposite to its point of entrance into the portal vein.

8. An anterior row of continuous suture is now placed, beginning at the cephalic end. Care should be exercised to avoid including the cutting suture. Either needle of the stay sutures may be used to place this suture. The anterior suture ends with a mattress suture around the free end of the second stay suture and both ends of the cutting suture.

9. The free ends of the cutting suture are now grasped firmly and the enclosed walls of the two veins gently sawed through between the two rows of continuous sutures, care being taken to avoid sawing too long with one length of suture.

10. After the cutting suture has emerged intact, the free end of the second stay suture and the needle end of the anterior suture are tied together, closing the opening left by the removal of the cutting suture.

After completion of the stoma the temporary ligature was tightened to occlude the portal vein. It was not tied but held tightly with a serrefine in order to prevent injury to the vein. The purpose of the temporary occlusion of the portal vein was to determine whether the stoma between the two veins would permit passage of all the portal blood. The patency of the stoma was indicated if the color of the intestines did not change after the ligature was tightened. As will be noted later, this temporary ligature was also used as a part of the procedure to establish permanent patency of the stoma.

After it had been demonstrated that the stoma was functioning properly, various lobes of liver were ablated. The left lateral and left central lobes were removed together in the following manner: The left lateral lobe was delivered into the operative wound and the left coronary ligament severed. The pylorus and duodenum were then covered with a moist towel and grasped by the assistant who exerted gentle, even traction caudally and to the left. Both left lobes of liver were then lifted forcibly and a curved hemostat was clamped securely across the pedicle common to the two lobes as near the other portion of the organ as space would permit. A second clamp was applied just above the first clamp and parallel to it. A dry gauze pack was placed around the clamped pedicle between the hemostat and the remaining portion of the liver. Both lobes were grasped firmly to prevent oozing of blood and severed close to the upper clamp with a scalpel. A double linen ligature was tied firmly around the tissue crushed by each clamp, the lower ligature being placed first. The debris of liver tissue and blood around the ligated pedicle was carefully sponged away. In some experiments the right central or gall bladder lobe was also removed. The technique was essentially the same as for the left lobes, except even greater care was necessary to prevent injury of the blood vessels to the remaining lobes and the cystic duct was clamped before section.

The technique of removal of lobes of liver in the dog is not difficult, but fatal accidents may happen if the various steps of the procedure are not carefully performed. The more common causes of accidents are the following: (1) Injury to the blood supply to the remaining portion of the liver, particularly the small papillary projection of the caudate lobe. It requires only a few grams of liver tissue without blood supply in the peritoneal cavity to produce death. (2) Severance of the vessels of the ablated lobes by tightening the ligatures before they are released from the clamps. These vessels are very thin-walled and fragile and when stretched can be easily cut with a ligature. (3) Permitting liver tissue without blood supply to remain at the site of section. Even a

very small amount of such traumatized hepatic tissue is dangerous to life. All of these accidents can be avoided if recognized and adequate care is taken to avoid them.

While the effect of partial removal of liver on the remaining portion of the organ is well known, in order to have comparative specimens, in many instances carefully controlled experiments were done. Animals of approximately the same size and weight were used. All operative procedures were performed at the same operative period. The same number of lobes of liver were removed from each, but in one a stoma was made between the two veins previous to removal of the hepatic tissue.

All the animals were given the same postoperative care and diet which maintained them in good condition throughout the period of observations. The condition of the liver in regard to restoration was determined at various periods of time after operation. Observations of the organ were made either at an exploratory operation or at necropsy. Not only was the liver carefully observed and weighed at necropsy, but the stoma between the two veins was also examined to determine whether or not it had remained patent.

Both animals in the paired experiments, those in which the operations were performed during the same operative period and in which the same number of lobes of liver were removed from each animal but the stoma between the portal vein and vena cava made in only one animal, were weighed and killed at the same time by bleeding under ether anesthesia and observations made and data secured as in the other experiments.

RESULTS

At necropsy of the first group of animals used in preliminary experiments performed to test the validity of the method for exploration of the problem, the livers of the animals in which the stoma between the two veins had been made were identical with those in which only hepatectomy had been done. Approximately the same amount of restoration of liver tissue had occurred in each group of animals. Examination of the site of operation on the veins disclosed the fact that the stoma was not patent. Since the opening between the two veins consisted of a single longitudinal slit, a pressure differential had to be developed which would be adequate to force blood through the narrow stoma. Evidently the increase in pressure in the portal vein owing to the loss of the portal vascular radicles contained in the liver tissue removed had not been sufficient to force blood into the vena cava when the usual technique for making an Eek fistula had been employed. Without the passage of blood through the opening, the cut surfaces of the walls of veins were left in apposition and healed together.

Another series of operations were performed in which the operative technique differed from that used in the first group in two respects:

- (1) The stoma was made as long as the anatomy of the veins would

permit.² The stoma thus extended from the hilum of the liver at the cephalic end to below the entrance of the renal vein into the vena cava at the caudal end. (2) The temporary ligature was kept securely tightened for several minutes after the lobes of liver were removed. Visual proof of patency of the stoma was obtained in several instances. In proper light the blood was seen through the thin wall of the portal vein flowing into the vena cava. The stoma was found to have remained patent in many of the animals in which this revised technique was used.

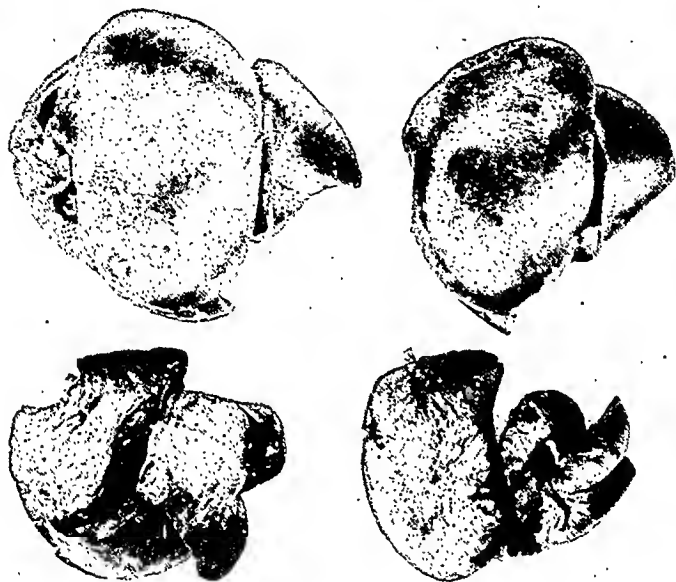


Fig. 1.—Specimens of liver obtained at operation and necropsy in a paired experiment. Animals were litter mates. Time between operation and necropsy was fifteen days. The date of operation and date of necropsy were the same for each animal. Specimen at top left weighed 387 Gm. and was obtained at necropsy from Animal 5a (Tables III and IV) from which the specimen at the bottom left, weighing 97 Gm., had been removed at operation. The specimen at the top right weighed 257 Gm. and was obtained at necropsy from Animal 5b (Tables III and IV) from which the specimen at the bottom right, weighing 123 Gm., had been removed and in addition a stoma was made between portal vein and vena cava. At necropsy the stoma was found to be patent but small. Note that restoration has occurred in each organ but is relatively slight in the presence of stoma.

Examination of the liver in the experiments in which the stoma remained patent revealed that the amount of restoration was less than in the control experiments. The remaining portion of the organ either had the same general appearance as it had at operation or showed relatively slight evidences of restoration. Its weight was but slightly greater than its estimated weight at operation (Tables III and IV, Fig. 1). The microscopic appearance of the hepatic tissue was normal. The method for estimating the amount of liver tissue left after hepatectomy used in this investigation was the same as has been employed in

TABLE III

COMPARISON OF RESTORATION OF THE LIVER AFTER PARTIAL REMOVAL IN ANIMALS WITH UNDISTURBED PORTAL CIRCULATION (A) AND IN THOSE WITH PATENT STOMA BETWEEN PORTAL VEIN AND VENA CAVA (B)

| NO. | BODY WEIGHT AT OPERATION (KG.) | BODY WEIGHT AT NECROPSY (KG.) | TIME BETWEEN OPERATION AND NECROPSY (DAYS) | ESTIMATED WEIGHT OF LIVER AT OPERATION (3.5% BODY WEIGHT) (GM.) | AMOUNT OF LIVER TISSUE REMOVED AT OPERATION (GM.) | ESTIMATED WEIGHT OF LIVER AT NECROPSY (3.5% BODY WEIGHT) (GM.) | WEIGHT OF LIVER TISSUE AT NECROPSY (GM.) |
|-----|--------------------------------|-------------------------------|--|---|---|--|--|
| 1a | 10.9 | 13.2 | 46 | 381 | 133 | 462 | 383 |
| 1b | 11.0 | 13.6 | 46 | 385 | 136 | 476 | 255 |
| 2a | 12.9 | 12.3 | 40 | 451 | 274 | 430 | 373 |
| 2b | 13.2 | 12.8 | 40 | 462 | 294 | 448 | 221 |
| 3a | 15.3 | 16.2 | 20 | 535 | 277 | 567 | 610 |
| 3b | 15.4 | 16.0 | 20 | 539 | 274 | 560 | 323 |
| 4a | 15.6 | 16.4 | 25 | 546 | 270 | 574 | 558 |
| 4b | 15.5 | 16.2 | 25 | 542 | 280 | 567 | 311 |
| 5a | 8.0 | 9.0 | 15 | 280 | 97 | 315 | 387 |
| 5b | 9.4 | 10.4 | 15 | 329 | 123 | 364 | 257 |

this laboratory for many years. It is admittedly only a rough approximation, but it is the best so far devised for the dog. Owing to the differences in the many breeds of dogs which reach the laboratory, this species cannot as yet be standardized as has been done with the rat. The method is based on a body weight-liver weight ratio and on the percental amount of liver tissue comprised in the various lobes as compared to the whole organ. McMaster and Rous found the liver weight to be 3.5 per cent of the body weight in dogs. In two series of our laboratory animals, each series consisting of 100 animals dying from causes not affecting the liver, the organ was found to comprise 3.45 per cent of the body weight. On the basis of these data the ratio of McMaster and Rous is used. The method of estimation based upon the

TABLE IV

DATA OBTAINED IN A PAIRED EXPERIMENT IN WHICH ANIMALS WERE LITTER MATES*

| | ANIMAL 5A | ANIMAL 5B |
|---|-----------|-----------|
| Body weight at operation | 8 kg. | 9.4 kg. |
| Estimated weight of liver at operation | 280 Gm. | 329 Gm. |
| Weight of liver tissue removed* | 97 Gm. | 123 Gm. |
| Weight of liver remaining | 183 Gm. | 206 Gm. |
| Body weight at necropsy | 9 kg. | 10.4 kg. |
| Estimated weight of liver at necropsy | 315 Gm. | 364 Gm. |
| Weight of liver at necropsy | 387 Gm. | 257 Gm. |
| Total weight of liver (amount removed added to amount obtained at necropsy) | 484 Gm. | 380 Gm. |
| Weight of new liver tissue formed | 204 Gm. | 51 Gm. |

*Hepatectomy only was done in Animal 5a; in Animal 5b a stoma was made in addition to partial removal of liver. Note that, while some of the figures are based on estimations, the total weight of liver (amount removed added to amount obtained at necropsy) is real and the difference found conclusive.

ratio of the weight of the various lobes to the total weight of the liver is even more unsatisfactory than the body weight-liver weight method. However, the left lateral and left central lobes of liver, those usually removed, are together approximately one-third of the organ and, with the addition of the right central lobe, more than one-half the liver.

COMMENT

The results of these experiments would appear not only to prove the conclusion reached in previous investigations that restoration of the liver after partial removal depends to a very great extent on the flow of portal blood through the organ, but also to suggest that the primary stimulus is the portal blood itself. While it would seem highly probable that, in the case of an organ with so many functions as the liver, there would be many stimuli, which, owing to a physiologic need, could cause restoration of hepatic tissue when it had been decreased below normal, the effect of such stimuli appears to be relatively slight compared to that caused by the stimulus of the portal blood flow and is secondary to the latter. While the restored liver tissue does actually compensate for a physiologic loss, its occurrence is apparently to establish an adequate portal pathway. The necessity for restoration of vascular channels appears greater than for the restoration of functioning hepatic tissue. It is quite possible that the stimulus and mechanism for the development of portal pathways through the remaining portion of the liver after partial removal, giving origin to restoration of the organ, are the same as those causing the formation of new areas of vascularization elsewhere in the body and the fact that the matrix happens to be hepatic tissue may be only a fortuitous circumstance. In this connection it should be noted that the control of the portal blood flow resides to a slight extent only in the liver but for the most part is located in the vasomotor controlled areas of the gastrointestinal tract and the other organs draining into the portal system. The liver has very little to say in regard to the amount of blood that passes through its portal channels.

The role of the portal circulation in the restoration of liver tissue after injury is not as definitely established as after partial removal of the organ. The procedure of removal of lobes of liver surgically is very simple compared to the destruction of liver tissue by hepatic poisons and infection. In the case of hepatic injury, other factors are operative in addition to the simple restoration of portal pathways and functioning hepatic tissue. The more important of these additional factors are the exciting agent which caused the injury and the processes of healing of the resulting lesion. In this complicated condition of the liver where physiologic and pathologic processes are occurring concomitantly, the significance of the flow of portal blood cannot be clearly discerned, but its importance cannot be doubted. Sufficient data are at hand to justify certain postulations. It appears highly probable that

restoration of hepatic tissue due to any particular agent continues, although possibly more or less imperfectly, until the portal pathways are partially occluded. Since the injury to liver tissue usually occurs in localized areas, the restoration is also localized. Each time a given hepatic area suffers injury, the vascular pathways are not completely repaired. Greater restoration occurs in those areas in which the hepatic cells and especially the vascular channels are least injured, giving rise to circumscribed masses of newly formed hepatic tissue. Finally, after repeated episodes of injury, the portal pathways become definitely restricted, greatly limiting or abolishing restoration. At this point the atrophic processes supervene.

Regardless of the cause and mechanism of restoration of liver substance, its occurrence is of great importance physiologically because there is thus assured a constant renewal of this vital tissue as long as the capacity for restoration persists. It is equally important pathologically. This remarkable characteristic of liver tissue must always be considered if the varying patterns of hepatic pathology are to be understood.

SUMMARY

The partial removal of the liver from a normal dog is followed by complete restoration of hepatic tissue within a fairly definite period of time. If a stoma is made between the portal vein and vena cava leaving both channels patent, thus permitting blood to interchange between the veins, at the same time the hepatic tissue is removed, restoration of the remaining portion of the organ is greatly decreased. The results of these experiments emphasize the importance of the portal circulation per se for restoration of the liver after partial removal. While there is evidence that stimuli other than the portal blood are operative in causing restoration of the liver, it has not been possible to determine the nature of such stimuli or to separate their action from that of the portal blood.

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WITH HOW LITTLE LUNG TISSUE IS LIFE COMPATIBLE?

REPORT OF A PATIENT FROM WHOM ALL PULMONARY TISSUE EXCEPT THE TWO UPPER LOBES WAS SUCCESSFULLY REMOVED

EVARTS A. GRAHAM, M.D., ST. LOUIS, MO.

(From the Department of Surgery of Washington University and the Barnes and the Children's Hospitals)

THE rapid development of thoracic surgery in recent years has made the extensive removal of pulmonary tissue technically feasible. The removal of a single lobe for bronchiectasis is now not only a common operation in the large thoracic clinics but it has also been made a relatively safe procedure with a mortality of 5 per cent or less. Even successful removals of a whole lung are now not unusual. Likewise, the removal of both lower lobes in cases of bilateral bronchiectasis has been performed on numerous occasions since Eloesser's¹ first case. Overholt⁴ in 1937 reported the removal of both lower lobes and the right middle lobe in four stages from a girl 19 years of age. Eight months after the operation the vital capacity was 1,162 c.c.

The case about to be described represents a still more radical removal of pulmonary tissue in that not only were the two lower and the right middle lobes removed but also the lingula of the left upper lobe. It is now generally accepted that the lingula is the homologue of the right middle lobe and that because of the anatomical distribution of the bronchus and blood vessels it should be regarded as essentially a separate lobe. From a practical standpoint, therefore, this case represents the removal of four of the six lobes, and, as judged by reports in the literature, it is the most extreme example of successful radical removal of pulmonary tissue. Although only two months have elapsed since the completion of the second operation, the boy is able to walk rapidly for short distances without dyspnea, and his vital capacity is 1,200 c.c. It is to be expected that his improvement will continue and that his vital capacity will increase.

Heuer and Andrus² state that in their experiments dogs were able to live indefinitely after the removal of all of the left lung and of the middle lobe of the right lung, with two lobes, therefore, remaining. In 1933, Heuer,² in reviewing his previous experimental work with Dunn, Andrus, Rienhoff, Cave, and other associates, stated, however, that he had found that in the dog life and good health were compatible with only one remaining lobe. In those experiments it was found that the pleural space created by the extensive removal of pulmonary tissue was obliterated very quickly (usually in about two weeks), chiefly by a

marked hypertrophy of the remaining portion of lung. The dog is admirably adapted for such a mechanism because of the extreme mobility of its mediastinal partition.

It has been uncertain how much one could apply to the human being the findings obtained on dogs. The human case to be described, however, may be regarded perhaps as a counterpart of Heuer's dog experiments in which only two lobes were allowed to remain, since the dog has six lobes of pulmonary tissue. The removal of four of the lobes, therefore, is practically equivalent to the removal in the human being of the two lower lobes, the right middle lobe, and the lingula of the left upper lobe.

Theoretically, since the tidal air requirement (500 c.c.) of an adult of average size is only about one-eighth of his vital capacity, it might be assumed that the surgical removal of about six- or seven-eighths of the total volume of the lung would be compatible with life. This might be the case if it were never necessary to use more air than ordinary tidal air requirements. It happens, however, that at times of active exercise and in periods of stress of various kinds more than the normal amount of tidal air is used. Dyspnea, therefore, would frequently be present if the individual were left with only about one-quarter or one-eighth of his normal pulmonary tissue. Fortunately the compensatory mechanism of hypertrophy of the remaining lung tissue occurs to relieve the situation. Actually, in the case here described, although four of the six lobes were removed, it would be unjustifiable to conclude that the patient was suddenly deprived of two-thirds of his pulmonary tissue. The long-standing disease had resulted in a shrinkage of those lobes which were removed so that there had been an opportunity for the two upper lobes to become hypertrophied. Moreover, more than a year elapsed between the removal of the lung tissue on the right side and that on the left, another factor inducing the hypertrophy of the right upper lobe.

An abstract of the case follows:

CASE REPORT.—This boy, aged 14 years, was first admitted to the St. Louis Children's Hospital on Oct. 10, 1938. The chief complaint was persistent cough with large amounts of purulent sputum. The parents stated that the present illness began with an attack of pneumonia at 2½ years of age. This was complicated by an empyema on the right side and a drainage tube was inserted after the removal of a portion of a rib. The drainage was maintained for about two months. Subsequently the empyema cavity and the thoracostomy incision healed satisfactorily. From then on the boy has never been well. Frequent attacks of so-called pneumonia occurred and at all times the productive cough continued. Sometimes he has coughed up small amounts of blood but he has never had a large hemorrhage. During the past two years he has been in somewhat better health except for the persistence of the cough and sputum. His physical condition, however, has prevented him from going to school as much as he should have. Three years ago he was in bed for two or three weeks with acute mastoiditis. About three weeks ago he

was sent to a tuberculosis sanatorium because his physician thought he might have tuberculosis. At the sanatorium, however, his condition was diagnosed as nontuberculous bronchiectasis.

Examination disclosed a slight discharge from the right ear and rather marked clubbing of the fingers. There was a moderate secondary anemia and a total leucocyte count of 15,500. Bronchograms showed the terminal divisions of the



Fig. 1.—Bronchogram showing bronchiectasis of right middle and lower lobes. The lipiodol filling of the lower part of the lower lobe is concealed somewhat in the print by the shadow of the diaphragm.

left lower lobe bronchi to be dilated and clubbed. The lingular division of the left upper lobe bronchus also showed bronchial dilatation. Similar changes were noted in the middle lobe bronchi of the right lung and there was an irregularity in the lumina of the right lower lobe bronchi. On the basis of the bronchograms an x-ray diagnosis was made of bronchiectasis involving the left lower lobe and the lingula of the left upper lobe, the right middle and the right lower lobes.

A bronchoscopic examination by A. Stutsman revealed as its only significant feature large amounts of pus coming from the lobes noted as diseased in the bronchograms.

It was decided to attempt to remove all of the diseased tissue. The decision to begin on the right side was arrived at because, in view of the fact that the empyema had been on that side, it seemed probable that the most active disease would be there.

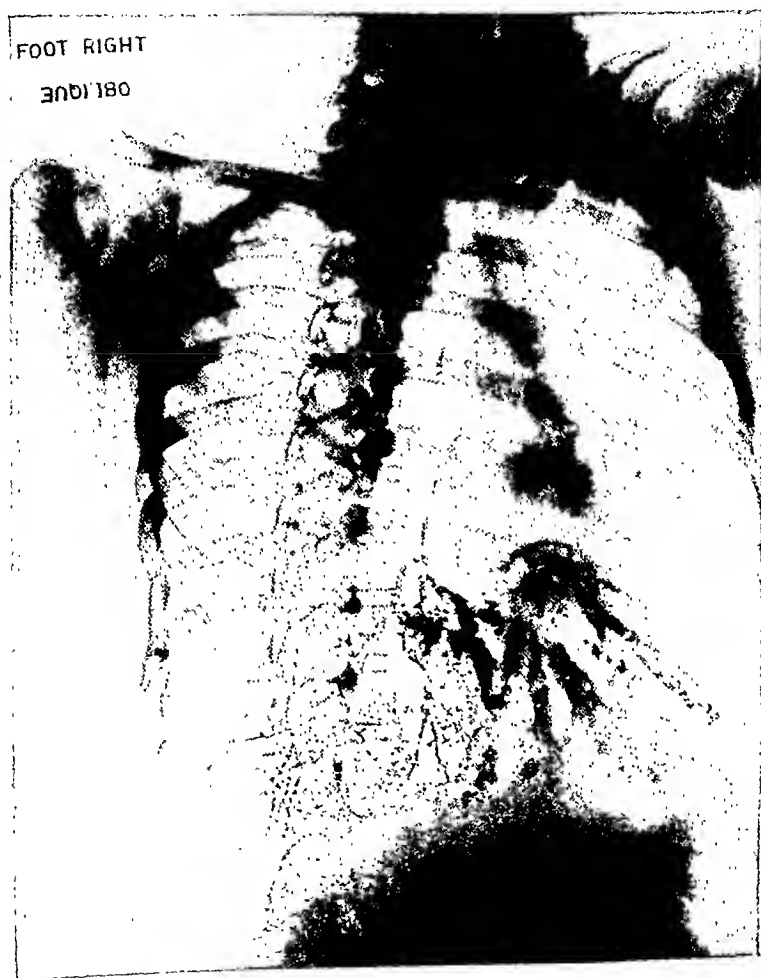


Fig. 2.—Bronchogram showing bronchiectasis of left lower lobe and of lingula of upper lobe.

The first operation was performed on Nov. 3, 1938. With intratracheal anesthesia with cyclopropane an incision was made beginning close to the spine at the level of the sixth dorsal vertebra which was brought down to the level of the seventh intercostal space and carried forward to about the anterior axillary line. The seventh and eighth ribs were found to be fused together as a result of the old empyema operation and it was necessary to resect both of them in order to enter the pleural cavity. The lung was firmly adherent to the chest wall by dense adhesions which required sharp dissection in order to mobilize the lower and middle lobes. The middle lobe was atelectatic and firmly adherent to the

mediastinal pleura. The interlobar fissure between the middle and upper lobes was incomplete and in order to free the middle lobe it was necessary to resect it from the upper lobe. Because the patient's condition was not entirely satisfactory it seemed advisable to complete the operation quickly and consequently a tourniquet was placed around the hilus of both the middle and lower lobes and the lobes were cut away. The stump was transfixed with No. 1 forty-day catgut and a mass ligation was made. Through stab wounds two rubber catheters were inserted through the seventh interspace into the thoracic cavity, one in approximately the midaxillary line, the other posteriorly in a line corresponding to the angles of the ribs. The wound was then closed in layers using pericostal sutures of No. 1 forty-day catgut to approximate the ribs as well as possible.

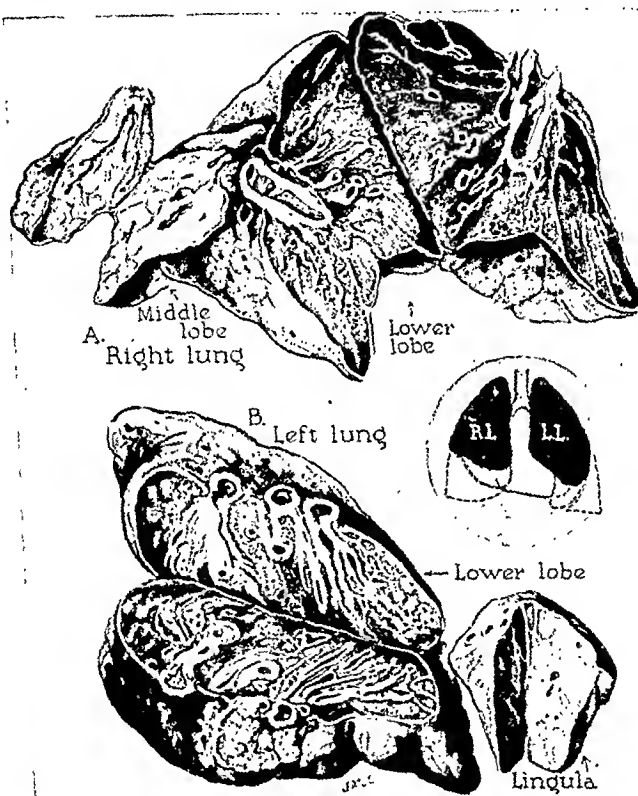


Fig. 3.—Drawing of removed portions of lungs after being cut open.

The skin was closed with a continuous dermal suture. When the operation was about two-thirds completed, the patient became cyanotic and his respiratory exchange was poor. Suction through the intratracheal catheter did not relieve the condition satisfactorily. Consequently, a bronchoscope was hastily passed by Dr. Stutsman and about 15 c.c. of thick purulent material tinged with blood was removed from the left main bronchus. A curved suction tip was then inserted into the various divisions of the bronchial tree which was well cleaned out. A marked improvement in the patient's condition was immediately noticed. After the completion of the operation another bronchoscopic aspiration was made before the patient left the operating room. He had also had a bronchoscopic aspiration in the operating room immediately before the operation was started. He, therefore, had three bronchoscopic aspirations in connection with the operation, one

immediately before, one during the course of the operation, and a third one immediately after the completion of the operation. It is probable that these were lifesaving measures. He developed a bronchial fistula and an empyema on the tenth postoperative day. He was discharged on Dec. 22 with the empyema cavity obliterated and the wound healed. He was still expectorating purulent sputum, but the amount was reduced about 50 per cent.

On Feb. 28, 1940, he was admitted to Barnes Hospital, rather than to the Children's Hospital, because he was then 15 years old. The interim history showed that since his operation he has been feeling much better. He states that

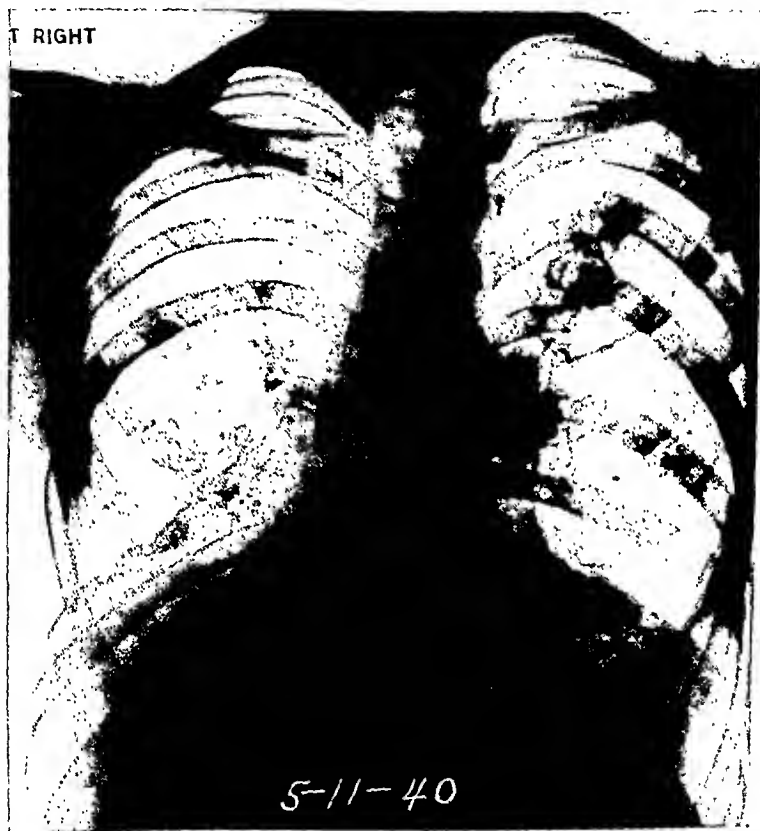


Fig. 4.—X-ray film at time of discharge after last operation.

he coughs only in the mornings and in the evenings. He was able to be in school continuously during the fall and winter of 1939. The right thoracotomy wound is solidly healed and gives no difficulty of any kind. A bronchoscopic examination by E. Kent on Feb. 29 showed a large amount of purulent secretion coming from the left lower lobe. A good view of the stump of the middle and lower lobe bronchus on the right side was available. The mucosa on the blind end was slightly hyperemic, but no other change was noted. On March 6 his second operation was performed. A bronchoscopic aspiration by Brian Blades was performed immediately before the operation was begun. Again under intra-tracheal anesthesia with cyclopropane an incision was made on the left side beginning at the level of the sixth rib close to its vertebral attachment and extending anteriorly over the level of the seventh and then the eighth rib to the anterior

axillary line. The sixth, seventh, and eighth ribs were divided close to their corresponding vertebrae and the pleura was entered in the seventh interspace. A partially atelectatic left lower lobe was found together with atelectasis of the lingula of the left upper lobe. A good many troublesome adhesions were found between the lower lobe and the diaphragm as well as between the lower lobe and the chest wall. Most of these required cutting between clamps. The inferior pulmonary ligament was followed to the root of the lower lobe. The interlobar fissure was also developed by blunt dissection to the root of the lower lobe. Individual ligation of the hilar structures was planned but abandoned for the tourniquet because of repeated respiratory difficulties which necessitated on several occasions the removal of the rib spreader and temporary closure of the chest wall. A tourniquet, therefore, was placed around the hilus of the lower lobe and a second tourniquet was placed about 3 cm. distal to the first. Amputation of the lower lobe was performed between them. A transfixion ligature of doubled No. 1 forty-day

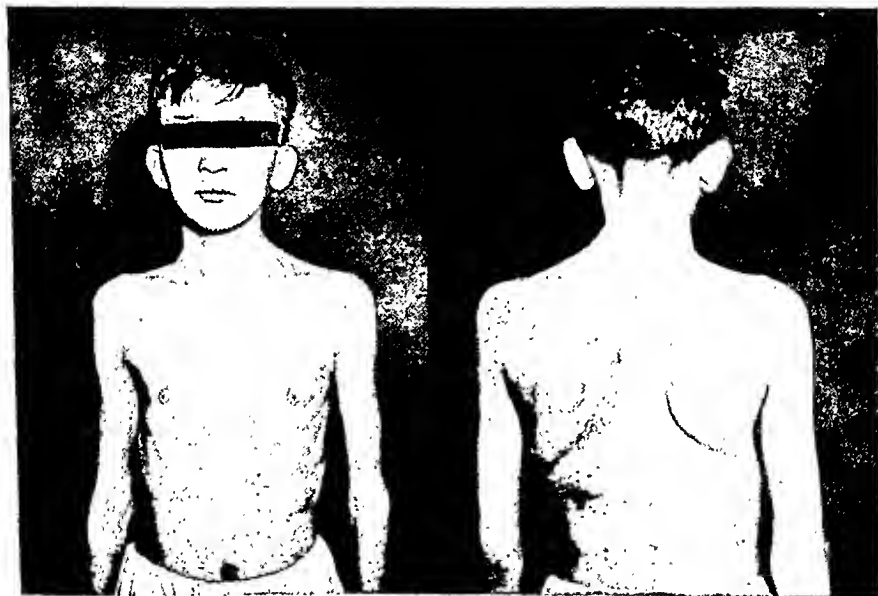


Fig. 5.

Fig. 6.

Fig. 5.—Patient at discharge after last operation.

Fig. 6.—View of back at discharge after last operation. Wounds solidly healed. Irritation of skin from adhesive plaster on left side gives erroneous impression of unhealed wounds.

chromic catgut was placed around the stump of the lower lobe which completely prevented any hemorrhage. It was also noted that the bronchus was tightly closed. Several reinforcing interrupted sutures of No. 1 twenty-day chromic catgut were placed through the open surface of the amputated hilus. The lingula was resected between clamps and the wound in the upper lobe repaired by the use of a continuous invaginating suture. Catheters were inserted through stab wounds in the anterior and the posterior axillary lines. The chest wall was closed by approximating the ribs with pericostal sutures of catgut and by bringing the severed ends of the ribs together with twenty-day catgut placed through drill holes. A flap of the longissimus dorsi muscle was brought over the posterior angle of the incision and retained with interrupted sutures of catgut. The soft tissues were closed in layers and the skin sutured with dermal. The patient had

another bronchoscopic aspiration by Dr. Blades immediately after the completion of the operation. He was also given a transfusion of 500 c.c. of blood although there had been no hemorrhage.

Evidence of an empyema appeared on the fourth postoperative day and a bronchial fistula was demonstrable on about the eighth day after the operation. On March 29 the diagnosis of a pericardial effusion was made both by fluoroscopy and kymography. The patient also at that time was very dyspneic. Aspiration at the right of the sternum in the fourth intercostal space yielded only 20 c.c. of bloody fluid which was sterile on culture. From then on his convalescence was uneventful and he was discharged from the hospital on May 11 with his wound solidly healed, the empyema cavity obliterated, no cough or sputum, no dyspnea on ordinary exertion, and a vital capacity of 1,200 c.c. For the first time in his memory he has been free from cough and sputum. The clubbing of the fingers has disappeared completely.

SUMMARY

A case is reported in which the two lower lobes, the right middle lobe, and the lingula of the left upper lobe were removed because of bronchiectasis. Its interest and importance lie in the fact that it demonstrates that a comfortable existence is compatible with only the right upper lobe and the left upper lobe without the lingula. It apparently represents the most extensive removal of pulmonary tissue so far reported in the human being. It is, therefore, a link in the chain of information gradually being accumulated which will enable us to tell how much lung tissue can be removed safely.

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STUDIES ON THE EFFECTS OF THE INHALATION OF A HIGH CONCENTRATION OF OXYGEN IN EXPERIMENTAL SHOCK*

GEORGE O. WOOD, M.D., M. F. MASON, PH.D., AND
ALFRED BLALOCK, M.D., NASHVILLE, TENN.

(From the Departments of Surgery and Biochemistry, Vanderbilt University)

THE fundamental pathologic change in shock consists of a discrepancy between the volume of blood in circulation and the capacity of the vascular bed, due to an increase in the capacity of the vascular bed or to a decrease in the volume of blood or to both. Regardless of the mechanism of the production of peripheral circulatory failure, a prolonged diminution in the effective blood volume results in tissue anoxia which is essentially that of the stagnant type. Most attempts at therapy have consisted of attempts to correct the disparity between the capacity of the vascular bed and the effective blood volume. Recently, attention has been directed again by Boothby, Mayo, and Lovelace¹ to the factor of anoxia in shock, and they have advised the inspiration of very high concentrations of oxygen in its treatment, especially during the early stages. Thus, they¹ administer pure oxygen routinely after major operative procedures, augmenting this with transfusions of blood when necessary.

The benefits to be obtained by the administration of a high concentration of oxygen have been outlined by Boothby and associates.¹ Thus, in the case of a retarded peripheral capillary circulation with the blood giving up as much as 80 per cent of its oxygen to the tissues, the capillary partial pressure of oxygen would fall from a normal of about 35 mm. to 14 mm. Hg. In this case the inspiration of 100 per cent oxygen, on the basis of the characteristic dissociation of oxyhemoglobin, could be expected to increase the amount of oxygen available to the tissues by as much as 50 per cent.

Our study was undertaken to determine, experimentally, the effects of the inspiration of these high concentrations of oxygen on moderate degrees of shock as produced by hemorrhage, histamine, and trauma.

METHODS

Dogs were used in all experiments. At a preliminary operation preparations were made for withdrawal of blood from sites which could not otherwise be readily approached. For this purpose an instrument² designed to permit withdrawal of portal venous blood without surgical exposure was inserted, and in addition the left kidney was explanted by the technique of Rhoads.³

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Morphine sulphate, 0.001 to 0.0015 Gm. per kilogram of body weight was administered at the beginning of all experiments. Approximately one and one-half to two hours later, under procaine infiltration anesthesia, the left common carotid artery was cannulated and connected to a mercury manometer, a maximum-minimum valve being used. Respirations were recorded by the tambour method. Hematoerit readings were made in duplicate with Van Allen tubes.

Shock was produced in the following manner. In the case of *hemorrhage* blood was removed in small amounts at frequent intervals until a quantity equal to about 2 per cent of the body weight had been withdrawn over a period of approximately two hours. This resulted in an acceleration of pulse rate, decrease in pulse pressure, and a slight decline in the systolic pressure. In the case of *histamine* the drug was administered subcutaneously in repeated small doses of from 1 to 4 mg. until the systolic pressure was fairly stationary at approximately 100 mm. Hg. The average total dosage was 6 mg. administered over a period of approximately two hours. *Traumatic shock* was produced by repeated blows with a hammer to the soft tissues of a hind limb, avoiding the region of the main vessels and nerves. General anesthesia was induced by ether during the period of actual trauma which usually lasted from two to five minutes. A systolic blood pressure of approximately 100 mm. Hg was reached in from one to four and one-half hours following traumatization, with the average elapsed time being approximately two hours.

The right external jugular vein, the explanted renal vein, and the femoral vessels of one leg were exposed under local anesthesia to facilitate withdrawal of blood samples. After the desired alteration in the circulation had been induced, blood samples for gas analysis were drawn anaerobically and without stasis from the portal vein, the renal vein, the femoral vein, the femoral artery, and the right heart in that order and as rapidly as possible. Blood from the right heart was obtained by means of a short cannula introduced through the right external jugular vein. Immediately following the taking of samples, a quantity of citrated blood equal to that which had been removed was introduced into the femoral vein. Oxygen was then administered by means of a Benedict spirometer containing the pure gas. Inhalation was continued for approximately fifteen minutes and shortly before the end of this period another set of blood samples was obtained. The blood gas analyses were performed with the Van Slyke-Neill manometric apparatus.

In a few instances whole blood pH determinations were made with the Coleman pH electrometer. In addition a few determinations of cardiac output were made by use of the Fick principle.

RESULTS

Experiments were performed on twenty-three dogs and the results of these are presented in Tables I, II, and III. In general, the most consistent results were obtained in those experiments in which shock was produced by hemorrhage. This is probably due to the fact that the degree of shock could be more easily controlled and that there were less marked fluctuations in the blood pressures of these animals.

Hemorrhage.—There were five experiments of this type. At the time of withdrawal of the first blood samples for gas analysis, there was an average depression of 45 mm. Hg in the systolic and 6 mm. Hg in the diastolic pressures. The average increase in pulse rate was 89 per minute. Following the administration of pure oxygen, the systolic arterial pressure rose an average of 6 mm. Hg and the diastolic pressures were usually unchanged. The average pulse rate decreased slightly and the respiratory rate usually remained the same.

During the administration of oxygen, the oxygen capacity decreased slightly in three experiments and increased slightly in two, the average being a slight decrease. Arterial oxygen contents were increased in all instances. The oxygen content of blood from the femoral vein was lower than that from other vessels in all experiments. It increased appreciably following the administration of pure oxygen in four experiments and decreased slightly in one. All renal and portal venous oxygen contents were increased by the inhalation of oxygen. The average oxygen content of mixed venous blood from the right heart also was increased. The average increase in oxygen content with oxygen inhalation was greatest in the blood from the portal vein. The order of increase in O_2 content of blood from other localities was, from greatest to smallest, the femoral vein, the renal vein, femoral artery, and the right heart. The average results of these experiments are presented in Table I.

Histamine.—There were seven experiments of this type. The average decline in blood pressure following the injection of histamine hydrochloride was 65 mm. Hg systolic and 22 mm. Hg diastolic. The average increase in pulse rate was 122 per minute. After breathing pure oxygen for a period of approximately fifteen minutes, the systolic pressure had risen an average of 7 mm. Hg and the diastolic pressure had risen an average of 9 mm. Hg. The pulse rate usually became slower and the respiratory rate remained approximately the same.

The average of oxygen capacities was slightly below that of the samples drawn just before administration of oxygen. The oxygen content of blood from the femoral artery rose in all instances; whereas, that of the femoral vein rose in six instances and fell in one, the average being an appreciable increase. The oxygen content of samples from the renal vein showed an increase in five experiments and a decrease in one (only six samples were obtained); whereas, the content

TABLE I
THE EFFECT OF THE ADMINISTRATION OF PURE OXYGEN ON SHOCK PRODUCED BY HEMORRHAGE (AVERAGES OF THE RESULTS OBTAINED IN 5 EXPERIMENTS)

| | B.P. IN MM. HG. | PULSE RATE PER MIN. | RESPIRA- TIONS PER MIN. | HEMATO- CRIT VOLUME % | O ₂ CAPACITY VOLUME % | CO ₂ AND O ₂ CONTENT, VOLUMES PER CENT | | | | | | | | | | |
|--|-----------------------|---------------------------|-------------------------------|--------------------------------|---|--|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|--|
| | | | | | | FEMORAL ARTERY | | FEMORAL VEIN | | RENAL VEIN | | PORTAL VEIN | | RIGHT HEART | | |
| | | | | | | CO ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ | O ₂ | |
| Controls | 170/99 | 76 | 51 | 43.8 | | | | | | | | | | | | |
| 118 min. after first bleed- ing; total blood removed equal to 1.65 per cent body weight | 125/93 | 165 | 17 | 46.6 | 23.78 | 32.60 | 20.75 | 45.87 | 7.64 | 35.35 | 18.18 | 39.70 | 12.52 | 40.65 | 11.03 | |
| After 15 min. of inspiring pure O ₂ | 131/94 | 150 | 18 | | 24.15 | 35.84 | 22.01 | 47.34 | 9.84 | 41.96 | 20.18 | 40.52 | 15.21 | 44.10 | 12.21 | |
| Average change resulting from the inhalation of O ₂ | +6/+1 | -15 | +1 | | +0.37 | +3.24 | +1.26 | +1.47 | +2.20 | +0.61 | +2.00 | +0.82 | +2.69 | +3.45 | +1.18 | |

of portal venous blood was increased in four and decreased in three experiments. Blood from the right heart was increased in oxygen content in five instances and decreased in two. There was a definite increase in the average content of the renal, portal, and right heart blood, but this increase was not as marked as in experiments dealing with hemorrhage. In addition, the individual increases in venous oxygen contents were much more variable. The order of increase in oxygen contents was from greatest to smallest, femoral vein, renal vein, right heart, portal vein, femoral artery. This is in interesting contrast to the results obtained in the experiments on the effects of hemorrhage. The average results of these experiments are given in Table II.

Trauma.—There were eleven experiments of this type. Trauma to one of the posterior extremities resulted in an average reduction of 67 mm. Hg in the systolic and of 19 mm. in the diastolic pressures. The pulse increased an average of 148 per minute. Administration of pure oxygen resulted in practically no change in blood pressure, but the pulse rate declined an average of 42 per minute. During the inhalation of oxygen, the average oxygen capacity fell slightly, while all arterial oxygen contents, with one exception, rose. The femoral venous oxygen content fell in three instances and rose in all others. Only eight renal vein blood samples were obtained and of these the oxygen content rose in six and fell in two, the average being an increase. Portal venous oxygen contents rose in all experiments except one. The average oxygen content of blood from the right heart was increased. On the whole the increase in oxygen content of blood from various sites was not as great as in the experiments on hemorrhage. The order of increase in oxygen content of blood from the various regions was, from greatest to smallest, the portal vein, renal vein, femoral vein, femoral artery, and right heart. This order of increase is, as were the changes in hemorrhage, quite different from that order obtained as a result of the administration of oxygen in histamine shock. The average results of these experiments are to be seen in Table III.

DISCUSSION

As has been shown, the administration of high concentrations of oxygen to dogs in shock usually results in an increase in the average oxygen content of both arterial blood and venous blood returning from various regions. The magnitude of the effects of this on the mean peripheral oxygen tension may be estimated by a consideration of the oxygen dissociation curve for dog blood,⁴ assuming, for the moment, constancy of hydrogen-ion concentration and that the mean venous oxygen tension is a function of the corresponding tissue tension. Under these conditions, in experiments in which shock was the consequence of hemorrhage, administration of oxygen resulted in an aver-

TABLE II
THE EFFECT OF THE ADMINISTRATION OF PURE OXYGEN ON SHOCK PRODUCED BY HISTAMINE
(AVERAGES OF THE RESULTS OBTAINED IN 7 EXPERIMENTS)

| | B.P. IN MM. HG | PULSE RATE PER MIN. | RESPIRA- TIONS PER MIN. | HEMATO- CRIT VOLUME % | O ₂ CAPACITY VOLUME % | CO ₂ * AND O ₂ CONTENT, VOLUMES PER CENT | | | | | | | | | |
|---|----------------------|---------------------------|-------------------------------|--------------------------------|---|--|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|
| | | | | | | FEMORAL ARTERY | FEMORAL VEIN | | RENAL VEIN | | PORTAL VEIN | | RIGHT HEART | | |
| | | | | | | | CO ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ |
| Controls | 164/93 | 77 | 52 | 32.8 | | 25.05 | 21.73 | 36.73 | 8.84 | 28.28 | 17.39 | 30.15 | 11.82 | 35.01 | 9.22 |
| 115 min. after first his- tamine injection; total of 6 mg. administered subcutaneously | 99/71 | 199 | 31 | 39.7 | 25.23 | | | | | | | | | | |
| After 15 min. of inspiring pure O ₂ | 106/80 | 178 | 34 | | 24.85 | 30.57 | 22.58 | 39.62 | 10.84 | 31.38 | 18.59 | 37.40 | 12.72 | 38.56 | 10.39 |
| Average change resulting from the inhalation of O ₂ | +7/+9 | -21 | +3 | | -0.38 | +4.92 | +0.85 | +2.88 | +2.00 | +3.10 | +1.20 | +7.25 | +0.90 | +3.55 | +1.17 |

*CO₂ content determined on rose bengal.

*CO₂ content determinations were made in 3 experiments only.

TABLE III
THE EFFECT OF THE ADMINISTRATION OF PURE OXYGEN ON SHOCK PRODUCED BY TRAUMA
(AVERAGES OF THE RESULTS OBTAINED IN 11 EXPERIMENTS)

| | B.P. IN MM. HG | PULSE RATE PER MIN. | RESPIRA- TIONS PER MIN. | HEMATO- CRIT VOLUME % | O ₂ CAPACITY VOLUME % | CO ₂ * AND O ₂ CONTENT, VOLUMES PER CENT | | | | | | | | | |
|--|----------------------|---------------------------|-------------------------------|--------------------------------|---|--|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|-----------------|----------------|
| | | | | | | FEMORAL ARTERY | | FEMORAL VEIN | | RENAL VEIN | | PORTAL VEIN | | RIGHT HEART | |
| | | | | | | CO ₂ | O ₂ | CO ₂ | O ₂ | %O ₂ | O ₂ | CO ₂ | O ₂ | CO ₂ | O ₂ |
| Controls | 176/100 | 72 | 66 | 34.3 | | 27.17 | 19.27 | 37.62 | 3.98 | 30.62 | 14.09 | 37.84 | 6.41 | 35.12 | 5.21 |
| 138 min. after trauma to the left posterior ex- tremity | 109/81 | 220 | 28 | 37.1 | 22.01 | | | | | | | | | | |
| After 15 min. of inspiring pure O ₂ | 108/79 | 178 | 33 | | 21.75 | 32.52 | 20.23 | 38.98 | 5.07 | 35.26 | 15.31 | 39.21 | 8.22 | 42.20 | 5.92 |
| Average change resulting from the inhalation of O ₂ | -1/-2 | -42 | 45 | | -0.26 | +5.25 | +0.96 | +1.36 | +1.09 | +4.64 | +1.22 | +1.37 | +1.81 | +7.08 | +0.71 |

*CO₂ determinations were made in 5 experiments only.

age estimated rise in oxygen tension of the femoral venous blood from 22 to 26 mm. Hg, an increase of 18 per cent. The estimated oxygen tension of renal and portal venous blood increased 20 and 17 per cent respectively. When histamine was employed to produce shock, the estimated oxygen tension of the femoral venous blood was increased 18 per cent; whereas, those of the renal and portal veins were increased 10 and 4 per cent respectively. Inhalation of oxygen in the experiments on traumatic shock resulted in an increase in the femoral venous oxygen tension of 13 per cent and an increase in the renal oxygen tension of 11 per cent. The oxygen tension in the portal vein was increased 19 per cent.

Although in making these calculations we have assumed constancy of blood hydrogen-ion concentration, actually this is not necessarily the case. In the first place gas analyses revealed that in most instances the CO_2 content of the blood rose during oxygen inhalation; and second, the fall in arterial pH accompanying this was directly measured with the glass electrode in several experiments, thus indicating clearly a considerable rise in alveolar CO_2 tension. Inasmuch as the absorbing power of the spirometer seemed adequate, it would appear that the respiratory resistance in our apparatus was responsible, although this is by no means certain. Similar evidences of progressive CO_2 excess were observed by Crafoord⁵ during administration of oxygen under positive pressure to dogs in the course of thoracic operations carried out under intravenous anesthesia.

Moderate increases in CO_2 tension, such as those in our experiments, might be expected to increase still further the availability of oxygen to the tissues (i.e., increase the average tissue oxygen tension). This is a consequence of the Bohr effect, that is to say, the effect of increased CO_2 tension in increasing the percentage of oxyhemoglobin dissociated at a given oxygen tension.

The coefficient of oxygen utilization is the fraction of the total oxygen content of the blood which is given up to the tissues in the passage of blood through the capillaries. It is calculated by dividing the arteriovenous difference in volumes per cent by the arterial oxygen content in volumes per cent. Normally, it varies considerably for different tissues and for the same tissue in accordance with the degree of its activity and rate of blood flow. Best and Taylor⁶ state: "Other things being equal, the slower the flow of blood through the capillaries the greater will be the quantity of oxygen given up to the tissues and the lower will be the oxygen content of the venous blood." Interpreted in terms of the coefficient of oxygen utilization, this means that, if the local tissue demand for oxygen remains the same, an increase in the coefficient represents a decrease in the rate of blood flow through the tissue and, conversely, a decrease in the coefficient represents an increase in the rate of flow. Referring to Table IV, it will

TABLE IV

THE AVERAGE CHANGE IN THE COEFFICIENT OF UTILIZATION OF OXYGEN RESULTING FROM THE INHALATION OF PURE OXYGEN*

| | POSTERIOR EXTREMITY | KIDNEY | INTES- TINES | BODY AS A WHOLE |
|--|------------------------|--------|-----------------|--------------------|
| Average change produced by inhalation of pure oxygen in shock produced by hemorrhage | -7% | -3% | -8% | -2% |
| Average change produced by the inhalation of pure oxygen in histamine shock | -8% | -3% | -3% | -5% |
| Average change produced by the inhalation of pure oxygen in traumatic shock | -5% | -3% | -9% | -3% |

*The coefficient of oxygen utilization is calculated by dividing the arteriovenous difference by the corresponding arterial oxygen content. The latter is corrected for changes in oxygen capacity occurring during the experiment.

be seen that following the administration of pure oxygen there was an appreciable decrease in the average oxygen coefficient of utilization for all the regions studied. This decrease could be the result of either a decrease in the metabolism of the tissue or an increase in the rate of flow through the tissue. The former possibility appears unlikely and we are led to believe that there was an increase in the rate of blood flow through all of the areas studied.

This apparent increase of flow in the various parts should be manifested by a rise in cardiac output and, indeed, such was found to be the case in experiments in which this function was measured.* According to Best and Taylor,⁶ an increased oxygen tension in the blood results in a slight diminution of the cardiac output; whereas, an increased carbon dioxide tension is usually accompanied by an increase in cardiac output. Sollman⁷ states that capillaries are constricted by excessive oxygen tension and are dilated by excessive carbon dioxide tension. Inasmuch as both an increase in oxygen tension and an increase in carbon dioxide content of the blood occurred in most of our experiments, it is impossible to determine which factor was dominant; however, it was noted that there was usually a slight rise in the blood pressure and a decrease in the pulse. This, under ordinary circumstances, would mean an increase in cardiac efficiency and probably in output.

If one uses the average decrease in oxygen coefficient of utilization (Table IV) as a very rough measure of the quantitative change in rate of flow, one sees that there are variations between the average change in rate of flow from the same regions in the different types of shock. In the traumatic and hemorrhagic types of shock, the average decreases in oxygen utilization by the different regions bear a strikingly

*The determinations of cardiac output made prior to oxygen inhalation were performed with an air-filled spirometer.

similar relationship to each other; in shock produced by histamine this relationship does not hold. Thus one finds that the presumed increase in rate of flow is much less marked in the intestinal region in those experiments in which shock was produced by histamine.

The difference in the response to oxygen therapy of shock as produced by hemorrhage and by trauma and that produced by the injection of histamine further emphasizes the view that the alterations in the circulation are not identical in these types of peripheral circulatory failure.

SUMMARY

1. The effects of the administration of pure oxygen to dogs with mild peripheral circulatory failure produced by hemorrhage, trauma, and injection of histamine have been studied.

2. The inhalation of oxygen under these conditions results in a considerable increase in the amount of oxygen available to the tissues, as evidenced by a rise in arterial oxygen content and increases in venous oxygen content of blood from various parts. This availability may be further enhanced by concomitant increases in carbon dioxide tension.

3. The observations confirm the prevailing impression that inhalation of high concentrations of oxygen exert beneficial effects in the treatment of peripheral circulatory failure.

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A TECHNIQUE FOR TOTAL GASTRECTOMY

ROSCOE R. GRAHAM, M.B., TORONTO, ONTARIO

(From the Department of Surgery, University of Toronto, and the Surgical Department of the Toronto General Hospital)

THERE are many physicians and a few surgeons who believe that the operation of total gastrectomy is a very questionable procedure. This is based upon the following data: first, there is a very high immediate mortality directly attributable to the operation; second, practically all patients who survive the operative ordeal ultimately die from metastases arising from the gastric carcinoma; third, the dietetic restrictions which many such patients must observe following survival from the operation of total gastrectomy are such as to be incompatible with happiness and freedom from gastrointestinal discomfort.

All who have struggled in attempting to solve this problem must accept the first two objections as being valid. The third, however, is debatable. It is true that some patients who have survived a total gastrectomy are unable to carry out a dietetic regimen which results in complete freedom from gastrointestinal symptoms. On the other hand, we have had patients who, apart from eliminating a few specific articles of diet from their menu, had a return of appetite and achieved freedom from gastrointestinal distress for as long as two and one-half years.

The enthusiasm which the individual surgeon displays for this operative procedure will depend largely on his philosophy of life. If such philosophy demands that all efforts be used to prolong life, even though the effort be accompanied by grave immediate risk, and though the patient ultimately must die from carcinoma, providing he lives long enough, then such a surgeon must be an advocate of total gastrectomy. Our experience with total gastrectomy in nineteen cases represents efforts to restore continuity between the esophagus and the rest of the gastrointestinal tract by many combinations and permutations of anastomoses between stomach, duodenum, and jejunum. The mortality until recently has been due almost entirely to the technical difficulty of securing a satisfactory esophagojejunal anastomosis. In one case in which the patient survived an esophagoduodenal anastomosis, he was never able to achieve as great gastrointestinal comfort as we would wish.

The preoperative preparation of patients who are possible candidates for total gastrectomy must be adequate. This demands the restoration of the fluid and salt balance and the correction of the avitaminosis which is almost invariably present, due either to the patient's inability to take an adequate diet or to the fact that a diet deficient in vitamins has been prescribed. The hazards of an associated anemia can be controlled by means of blood transfusion.

Despite our belief that this operation is justifiable, the high primary operative mortality has made us pause, on many occasions, to question whether we were justified in asking patients to accept such an operative risk; yet, when it is realized that without excision of the carcinoma a distressing death awaits the patient, the attempt to relieve the symptoms becomes justifiable. The technique which is presented has been carried out in six cases, and in none of these has the primary cause of the still appalling primary mortality been due to the esophagojejunal anastomosis. One patient died of peritonitis, due to obstruction of the distal jejunum, the result of a jejunostomy which obstructed the jejunum. This obstruction resulted in a ballooning of the proximal jejunal limb to such a degree as to result in a leak at the esophagojejunal line of anastomosis. The second patient died from anuria following a transfusion. This unfortunate and still unexplained reaction occurred despite the most meticulous care in the laboratory in carrying out tests for determining compatibility of donor and recipient bloods. One patient died from coronary thrombosis when convalescent. One died from acute pancreatitis, the result of damage to the pancreas following a partial resection of this organ, which was involved in the neoplasm. One patient is still alive and well nineteen months after operation. A recent patient died forty-eight hours postoperatively, and this is the only case in which it was impossible to secure a post-mortem examination, and it is believed that this death was due to an overwhelming respiratory infection.

Of the other thirteen cases, there were four survivals. Three died of cardiovascular accidents, one of a cerebral embolus on the tenth postoperative day. This patient had a coincident removal of the spleen, and it would appear that the vascular accident was contributed to by the increase in platelets which followed the splenectomy. Since this experience we have avoided removal of the spleen wherever possible, despite the fact that the coincident removal of this organ greatly simplifies the technical procedure. If, because of accidental injury of the splenic blood supply, or because of the site of the growth splenectomy becomes necessary, the patient should be given heparin postoperatively in an effort to prevent a repetition of such an unfortunate vascular accident. One patient died of hemorrhage which came on suddenly forty hours postoperatively. Only one patient had a subphrenic infection, which occurred six weeks postoperatively, the result of a leak at the anastomosis. The other deaths were due to a leak at the esophagojejunal anastomosis.

This terrific mortality is not such as to make one proud of the results. It is presented to show the tenacity of purpose which is prompted by the firm belief that every effort should be made to extirpate a gastric carcinoma which, if left in situ, is inevitably fatal. This attitude

is further justified by the fact that in seven of these nineteen cases, or 36.8 per cent, there was no evidence of extension of the disease beyond the stomach and no metastatic disease in the adjacent lymph glands. The fact, then, that over one-third of the cases of gastric carcinoma are lethal solely because of the local extent of the disease, justifies the hope that a survival following a total gastrectomy may result in a prolongation of life, freedom from gastrointestinal distress, and a mental peace which will justify the high primary operative mortality. It is hoped that our future efforts as a result of the technical procedure to be presented may result in a lower mortality. This hope is justified by our experience with the last six cases, in which in only one instance was the anastomosis a factor in the ultimate mortality, and this only indirectly, because of a technical error in the performance of a jejunostomy.

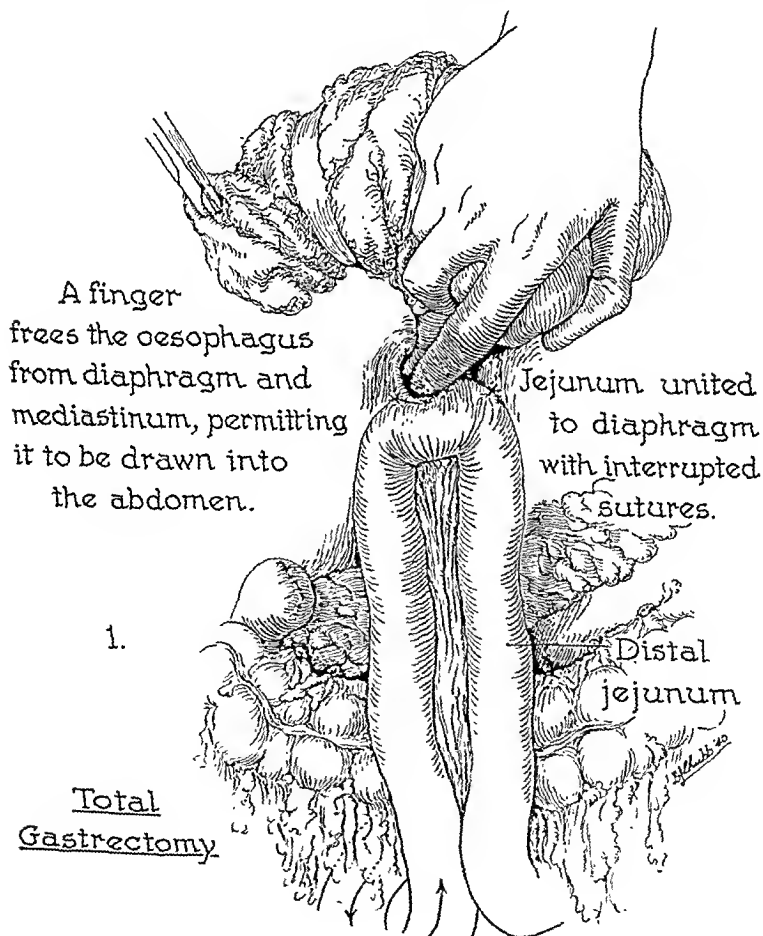


Fig. 1.—The stomach has been divided from the duodenum. The illustration shows the method of increasing the infradiaphragmatic length of the esophagus by freeing it from the margins of the diaphragm by inserting the finger along the esophagus into the mediastinum. The esophagus at a point eighteen inches from the duodenojejunal juncture is fastened to the diaphragm behind the entrance of the esophagus by means of interrupted sutures.

DETAILS OF THE OPERATIVE PROCEDURE

The abdomen is opened by displacing the upper right rectus laterally by a right paramedian incision. A survey of the intraperitoneal lesions must be carried out before any further direct attack on the gastric neoplasm is made. Particularly one must be certain that no metastases are present in the pouch of Douglas in the female, or in the rectal shelf in the male; that the liver is free from metastases; that the carcinoma has not invaded surrounding structures; that the glandular involvement is not so extensive as to be incapable of removal. If the disease is limited to the stomach and adjacent lymph glands, and the involvement of other structures does not preclude its excision, then adequate exposure must be provided. Transverse divi-

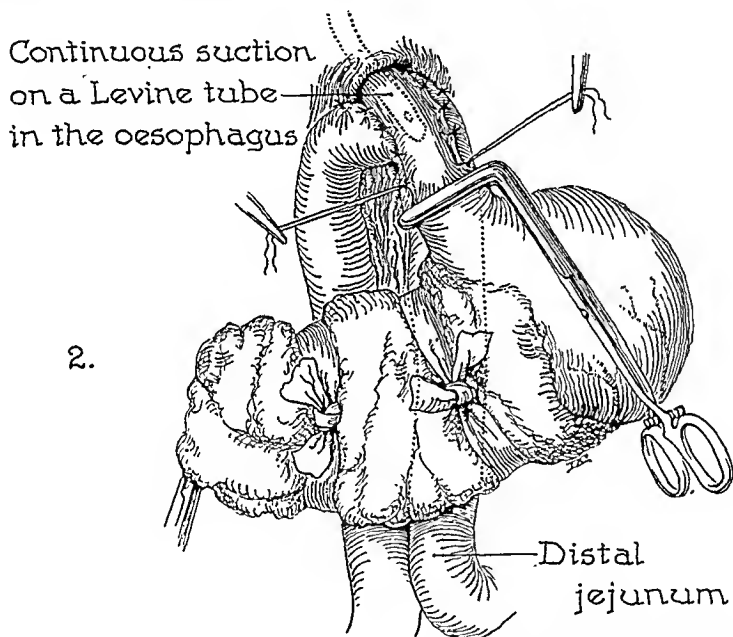


Fig. 2.—The infradiaphragmatic portion of the esophagus is placed on the anterior surface of the distal limb of the jejunum and fastened there by means of interrupted silk sutures. The Levine tube in the esophagus by means of attachment to suction apparatus keeps the esophagus free from accumulated secretions.

sion of the left abdominal wall midway between the ensiform and the umbilicus is a great asset. The maneuver of mobilizing the left lobe of the liver as popularized by Turner adequately exposes the entrance of the esophagus to the peritoneal cavity. The great omentum is removed in its entirety and the greater and lesser curvatures of the stomach mobilized and the duodenum divided just distal to the pylorus. The technique of this mobilization and closure of the duodenal stump has been previously presented.¹ When the stomach has been freed from the duodenal end, it is wrapped in gauze which is tied with heavy

tape. By downward traction, using the stomach as a handle, the finger is inserted between the esophagus and the opening of the diaphragm. This will isolate both vagi, the division of which will permit the mobilization of the esophagus to a surprising degree. Further separation of the periesophageal structures by blunt gauze dissection will often make it possible to draw down the esophagus a distance of two inches below the opening in the diaphragm. When this has been accomplished, the suggestion of Allen² of suturing the jejunum to the under-surface of the diaphragm by means of interrupted sutures is carried out (Fig. 1). A point in the jejunum approximately eighteen inches from the duodenojejunal junction is selected and the jejunum is brought up in front of the transverse colon to be fixed to the diaphragm. The procedure advocated by Allen adequately fixes the

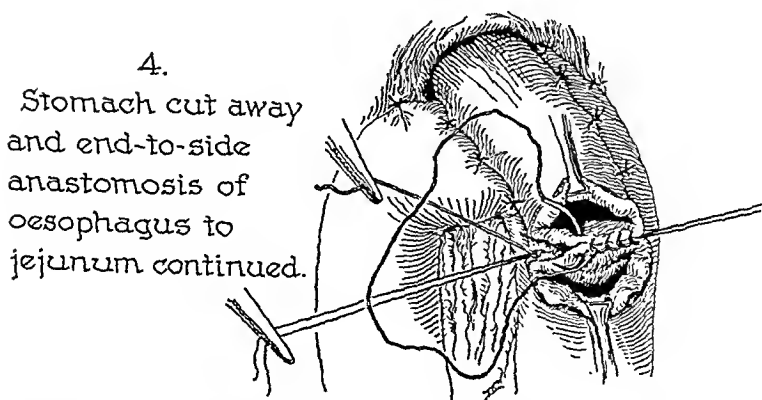
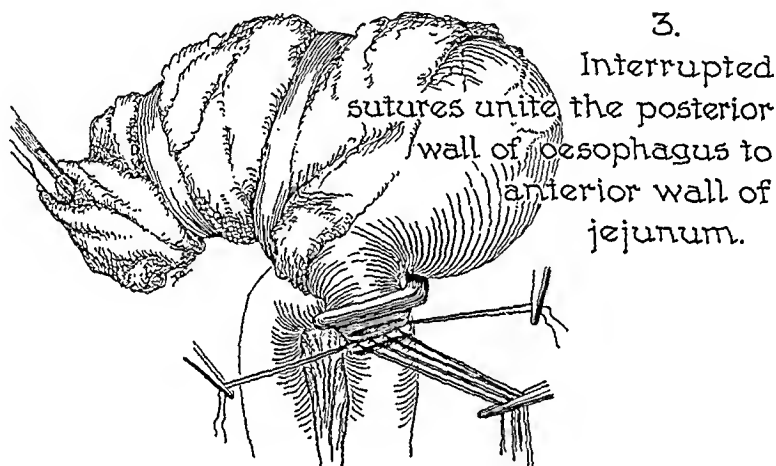
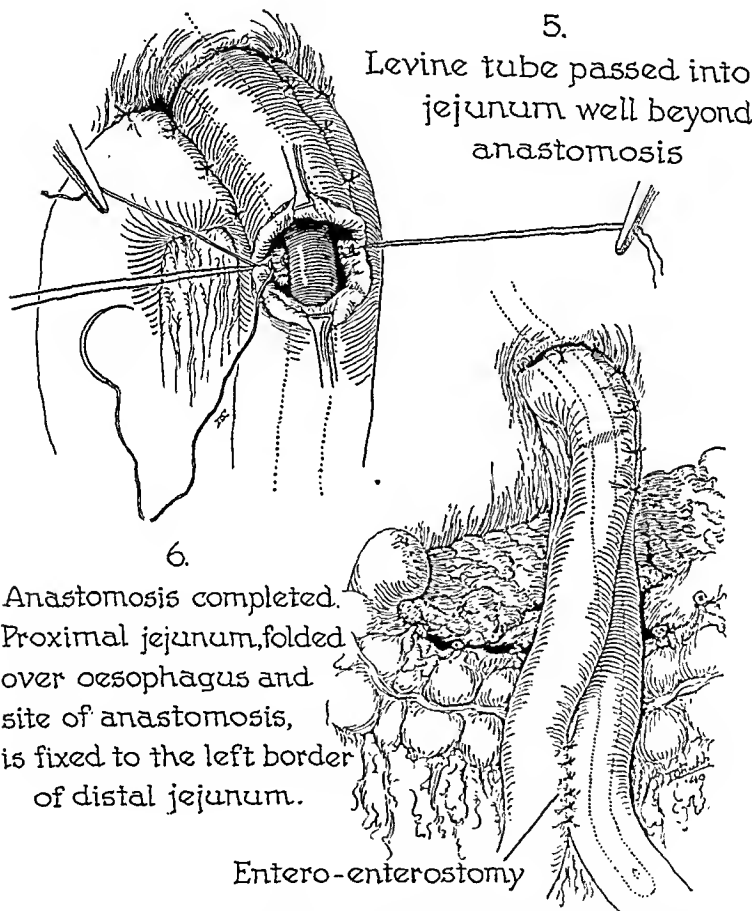


Fig. 3.—If the infradiaphragmatic portion of the esophagus is unduly short, it is advantageous to leave the stomach attached to the esophagus while interrupted sutures unite the posterior wall of the esophagus to the anterior wall of the distal limb of the jejunum. The two lateral sutures are held in hemostats and act as stay sutures while the esophagojejunal anastomosis is completed.

Fig. 4.—Here the stomach is cut away and the mucous membranes of the stomach and jejunum are being united.

jejunum and prevents the weight of jejunal contents from being a factor in creating tension on the new esophagojejunal anastomosis. When the jejunum is firmly anchored to the diaphragm, the infradiaphragmatic portion of the esophagus is then fixed by means of interrupted sutures to the anterior surface of the distal limb of the jejunum. Usually three or four such sutures on either side are sufficient to achieve this, the most distal suture on either side being held in hemostats to act as guy sutures (Fig. 2). The esophagus then may be divided, great care being taken to keep up continuous suction by a Levine tube which had



Figs. 5 and 6.—When the posterior layer of mucous membrane sutures is completed, the Levine tube is passed down further into the distal jejunum well past the esophagojejunal anastomosis and the anterior layers of the anastomosis are completed. The proximal jejunum is then folded over the front of the esophagus and the esophagojejunal anastomosis and united to the lateral margin of the distal limb of the jejunum. By this maneuver the esophagus and the esophagojejunal anastomosis are completely encircled by the jejunal loops. This contact of peritoneum to peritoneum ensures healing to a greater degree than the contact of the bare esophagus to the jejunum. This maneuver completely obstructs the proximal jejunal loop and makes an entero-enterostomy necessary. During this anastomosis the Levine tube is passed further down into the distal jejunum to make possible direct jejunal feeding early in the patient's convalescence.

been passed into the stomach before the operation, and which is now withdrawn to a point in the esophagus just proximal to the line of division. If it has been possible to bring down only a short infra-diaphragmatic portion of the esophagus, it may be advantageous to retain the stomach as a means of downward traction while interrupted sutures unite the posterior wall of the esophagus to the anterior wall of the jejunum (Fig. 3). The esophagus then must be divided and the jejunum is opened. The Levine tube is then passed down into the

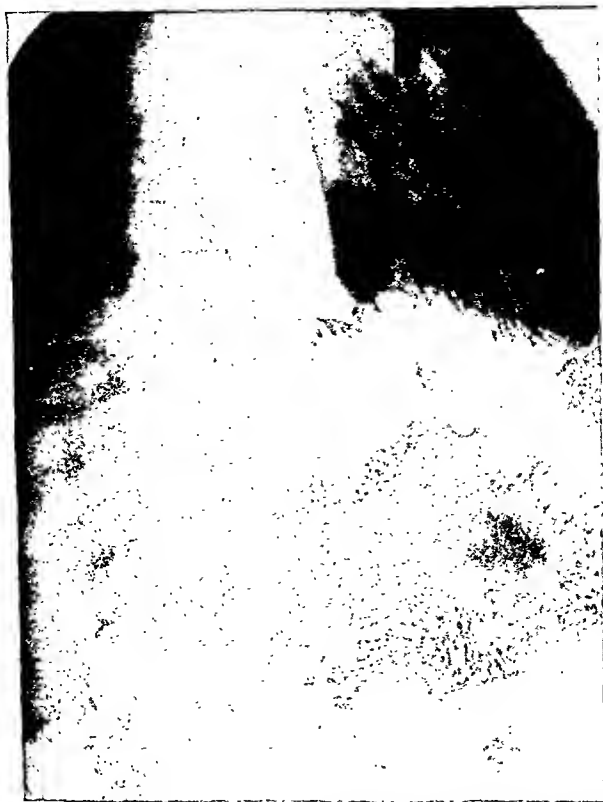


Fig. 7.—Case of Mrs. C. B. (No. A51111), total gastrectomy, July, 1938. X-ray study, Aug. 15, 1938, showed evidence of efficient anastomosis. Alive and well, February, 1940.

distal jejunum after the posterior layer of the anastomotic suture has been completed (Fig. 4). The anterior layers of the anastomosis are completed in the usual manner, making a very satisfactory end-to-side stoma between the lower cut end of the esophagus and the anterior wall of the distal limb of the jejunum. When the anastomosis is completed, the proximal jejunal loop is then rolled laterally across the esophagus and sutured to the left lateral margin of the distal limb of the jejunum. This completely surrounds the infradiaphragmatic portion of the esophagus with the jejunal loops, and very firmly covers and supports the end-to-side jejunoesophageal anastomosis, as indi-

eated in Fig. 5. This maneuver completely obstructs the proximal jejunal loop, and therefore an enteroenterostomy must be carried out between the proximal and distal jejunal loops. During the performance of this anastomosis, the Levine tube is passed on into the distal limb of the jejunum past the enteroenterostomy (Fig. 6). The abdominal wall then may be closed in layers without drainage. A stitch placed in the patient's cheek is tied around the indwelling Levine tube, in order that the patient's immediate postoperative restlessness will not result in removal of this tube. While the interrupted sutures indicated in the text and in the diagrams may be accomplished by means of catgut sutures, I prefer to use silk. The minimal trauma and tissue reaction about silk commends it to a very great degree in this operation.

Immediately following operation, the fluid balance is maintained by means of the intravenous administration of 5 per cent glucose in saline solution and 5 per cent glucose in distilled water, 1,500 c.c. of each in twenty-four hours. Five hundred cubic centimeters of blood are given during the operative procedure. No food or fluid is given by mouth, but the patient is allowed to take ice chips. The oral cavity is sprayed with liquid paraffin, which adds greatly to the patient's comfort by avoiding a dry mouth, and it also allays the irritation from the indwelling Levine tube. In addition it is a real factor in the prevention of postoperative parotitis. At the end of twenty-four hours 10 per cent glucose in saline solution can be introduced into the jejunum through the Levine tube by the drip method at the rate of 125 c.c. an hour. At the end of forty-eight hours, the type of feeding and management as advocated in the tube treatment of gastric ulcers is applicable here.¹ The x-ray appearance of the anastomosis is shown in Fig. 7. This patient was operated upon July, 1937, and to date is well and free from recurrence and suffering no gastrointestinal distress.

CONCLUSIONS

1. Over one-third of the patients submitted to total gastrectomy had no histologic evidence of metastasis in the regional lymph glands or in other intraperitoneal structures.

2. Such an incidence of local disease justifies the operation of total gastrectomy, despite the high primary postoperative mortality.

3. The survival from this procedure is compatible with happiness, negligible dietetic restrictions, and freedom from gastrointestinal distress.

4. The technique of esophagojejunal anastomosis here presented offers a method which, it is hoped, will decrease the immediate postoperative mortality.

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THE SURGICAL TREATMENT OF PRIMARY DUODENAL DIVERTICULA

JOHN J. MORTON, M.D., ROCHESTER, N. Y.

(From the Department of Surgery, the University of Rochester School of Medicine and Dentistry)

THE history of the surgery of primary duodenal diverticula is a relatively recent one. It dates back for only twenty-five years when Forsell and Key¹⁷ performed the first deliberate attack on a primary duodenal diverticulum. Diverticula secondary to duodenal ulcer had been recognized and treated for a longer period. Here, however, the operation was directed against the ulcer, and the associated diverticulum was a mere incident.

Although primary duodenal diverticula are relatively common, indications for surgery upon them have not been of great frequency. In the University of Rochester Hospitals primary diverticula of the duodenum have been recognized in at least thirty-three individuals but operation has been performed in only two instances.

CASE REPORTS

CASE 1.—I. B. (No. 161042), a 57-year-old woman, was admitted to the Strong Memorial Hospital on Jan. 12, 1940. For the past eight or nine years she has had frequent attacks of dull aching in the right upper quadrant. The pain radiated to the right posterior chest wall and right shoulder. During the last two months the attacks had increased in frequency, severity, and duration. The distress was almost constant although mild. The only other symptom noted was frequent gaseous eructation. In her past history the patient had an appendectomy and bilateral salpingo-oophorectomy twenty-nine years ago. There were attacks of renal colic and pyuria ten years ago.

Examination was negative with the exception of an area of tenderness on deep pressure in the right epigastrium just above and slightly lateral to the umbilicus.

Laboratory examinations showed a rather large gall bladder with poor emptying after a fatty meal. There were no stones visualized. The gastrointestinal series revealed a diverticulum of the descending duodenum (4.5 by 5 cm.) with no retention of barium. On fluoroscopic examination the tenderness previously noted was found to be directly over this diverticulum. The diverticulum seemed to be close to the region of the common duct entrance. There were also several olive-sized diverticula of the first jejunal loop made out.

At operation, the gall bladder appeared to be normal. At least six diverticula were demonstrated in the jejunum. These had no evidences of inflammation or obstruction. The duodenum was mobilized by dividing the peritoneum along its lateral edge and rotating the viscus toward the midline. The diverticulum was demonstrated. It was freed from its position between the common duct and head of the pancreas until it could be brought into the peritoneal cavity at the right side of the descending duodenal loop. The mouth admitted the index finger readily. The superior pancreaticoduodenal artery ran over the neck of the sac. The opening was intimately associated with the papilla of Vater. It was com-

sidered better surgery to treat this diverticulum conservatively. Accordingly it was left in situ in the belief that it would not trap duodenal contents and would no longer exert pressure on the common duct junction.

Postoperatively the patient made a good recovery. She has been free from symptoms for two months. Time will tell whether the surgeon's judgment was good.

CASE 2.—R. D. (No. 104466), a 60-year-old woman, was admitted to the Strong Memorial Hospital on Dec. 10, 1939. Two days previously she had a sudden onset of severe epigastric pain, starting shortly after breakfast. It was crampy in nature and centered more in the right upper quadrant. It was accompanied by chills, fever, and vomiting. There was radiation of pain to the back but not to the right shoulder. The pain subsided in five hours, but anorexia, malaise, fatigue, and nausea persisted. The skin was noted to become yellowish. The urine was dark; the stools were not observed. There was no previous history of similar nature. The rest of the history had no bearing on this illness.

Examination showed an acutely ill, irritable, drowsy person with moderate icterus. There was tenderness in the right upper quadrant but no spasm. The examination was negative in other respects. The temperature was normal, the pulse was 80. Positive laboratory findings were bile and acetone in the urine. The icteric index was 13. Cholecystogram showed poor concentration of the dye but nothing that could be interpreted as gallstones. Gastrointestinal series demonstrated a small diverticulum (4 by 4.5 cm.) of the descending loop of the duodenum. There was also a large diverticulum (4.5 by 6 cm.) coming off the ascending portion near the ligament of Treitz. There was tenderness over this latter diverticulum, and retention of barium at the four-hour examination. Diagnosis: Cholecystitis probable; diverticula of the second and third portions of the duodenum. The patient's acute symptoms quickly subsided on a smooth low fat diet and atropine. She was discharged ten days after admission. She was readmitted on Feb. 27, 1940. In the interval she had remained weak and was slow in regaining her strength. She began to feel better about one week before this second admission. Four days before, she had another attack of severe epigastric pain, lasting five hours. It required morphine for relief. There was no vomiting but persistent nausea. No icterus was noted. She has had headaches and soreness between the shoulder blades. Upon examination there was tenderness in the right upper quadrant, but nothing else of significance.

At operation, a thickened gall bladder was removed. It contained stones. The diverticulum of the third portion of the duodenum was exposed by dividing the gastrocolic omentum and entering the lesser peritoneal sac. The fourth portion of the duodenum was isolated. The pancreas was lifted up from it and the duodenum traced to its third portion. At this place the neck of the diverticulum was isolated. The pouch was freed, the neck of the sac divided. The defect was closed first with a Parker-Kerr stitch and then with a purse-string suture inverting the mucosa. A third layer of interrupted silk sutures in the serosa was used. Operation was done by Herman Penrose.

Recovery was uneventful. Patient is well to date.

It is apparent from a close study of these two records that perhaps in these cases operation was necessary because of other pathologic states. In Case 1 there was a mechanical factor of back pressure on the common duct. The patient had been told elsewhere that she had a diseased gall bladder. This, coupled with her fear that it was malignant, made an exploration almost obligatory. In Case 2 the presence of a pathologic

gall bladder probably accounted for the symptoms. The diverticulum was removed in order to eradicate a potential source of danger.

A review of the literature on this subject leaves an impression that primary diverticula of the duodenum in most cases do not cause symptoms. The majority of the diverticula arise in the region of the ampulla of Vater. The outpouching occurs through a potentially weak area in people beyond 25 years of age, most frequently in the late 40's or 50's. The opening is usually large; the sac empties easily because it has dependent drainage. The position of the sac is nearly always retroperitoneal and on the concave side of the duodenal loop. There is thus a support from the peritoneum, the pancreas, and the duodenal wall itself so that these herniations cannot easily sag or kink at the neck of the sac until they have attained a large size. Some of them are completely surrounded by pancreatic tissue. They may contain accessory pancreatic tissue in their walls.

There is evidence, however, that in some instances symptoms have been due to the diverticulum. There are enough well-documented cases to indicate that removal of the diverticulum has been followed by a complete absence of the distress which prompted operation. In such cases symptoms may have followed a gastric, duodenal, biliary, pancreatic or intestinal stasis pattern. Typical examples can be quoted in support of each of these. There is thus no definite clean-cut picture by which a clinical diagnosis can be established. But, if such a patient with symptoms referable to the upper abdomen can be shown to have negative examinations for the stomach, duodenum, biliary tree, pancreas, and upper intestine, the diverticulum may then be presumed to be at fault. If also it can be shown to have tenderness over it on fluoroscopic examination and stasis of the barium in its sac, the evidence becomes stronger. In some cases the duodenum above the diverticulum may show evidence of partial obstruction. This is manifested by dilatation of the loops, an upset in the peristaltic regularity, and perhaps pylorospasm.

The presence of inflammation can manifest itself as a localized diverticulitis; or as an extension into the biliary tract, pancreas, or adjacent structures. This may give rise to secondary cholangitis or cholecystitis, pancreatitis, etc.^{2, 6, 19} The presence of jaundice has been noted frequently in these cases. Diverticulitis may be catarrhal, suppurative, gangrenous. There have been perforations with local abscess or peritonitis (Table V).

Finally, there is a remote chance of neoplastic change in a duodenal diverticulum. Morrison and Feldman²² described a carcinoma in such a case; and Mendillo and Koufman,²⁸ a leiomyosarcoma in another.

There is a justification for surgery of duodenal diverticula upon the following grounds: (A) mechanical: (1) giving rise to symptoms from

local stasis in the diverticulum, (2) giving rise to symptoms from partial obstruction to the biliary tract, pancreatic ducts, or duodenum; (B) inflammatory: (1) local diverticulitis, perforation, abscess, peritonitis, (2) secondary inflammation of the biliary tract (jaundice), pancreas, duodenum, retroperitoneal tissues; (C) neoplastic change.

It is possible also that the presence of diverticula may upset the smooth running of the gastrointestinal tract by disturbances in the nervous control.

Operations upon duodenal diverticula have been of several different types. First of all, in very difficult cases a direct attack may be avoided by resorting to a side-tracking operation. This has been the solution used by many well-known surgeons, no attempt being made to expose the diverticulum. Such operations as pyloric division with a Polya type of anastomosis have been done. In the absence of a pathologic lesion in the antrum or in the first part of the duodenum such an operation is not to be recommended.

Direct approach to the diverticulum varies with its situation. When the diverticulum is in the descending loop (second portion of the duodenum), its position is nearly always retroperitoneal. It frequently is peri-Vaterian and in close relationship to the openings of the common duct and the pancreatic ducts. At times it is embedded in the pancreas. It is on the concave side of the loop and posterior. Many times the main pancreaticoduodenal vessels run directly across the neck of the sac. In a number of instances surgeons have failed to find such a diverticulum at operation. This was more frequent when these cases were first being explored.

The approach from the medial side of the duodenal loop is difficult and annoying. There are many small vessels entering the tissues about the head of the pancreas. Nevertheless some surgeons have made this approach successfully, even dividing the pancreas over the sac in order to identify it.

The approach from the lateral border of the duodenum is better. The peritoneum is divided along the lateral border of the duodenum. This is a relatively bloodless area. The surgeon then mobilizes the duodenum towards the midline. He can turn it over, exposing the posterior wall. The duodenum can be exposed posteriorly all the way to Treitz's ligament in this manner. It is the type of approach recommended by Ladd³¹ and by Morton and Jones³² for congenital duodenal obstructions. If very small the diverticulum can be inverted without excision.²² If larger, the diverticulum is freed from the surrounding tissues by careful dissection. The neck is ligated, the sac excised, and the stump inverted into the duodenum. Reinforcing sutures may be used. When the neck is wide the defect may be closed in a transverse direction. The pancreaticoduodenal vessels may be pushed aside and

preserved. If the opening of the sac encroaches upon the ampulla, it may be dangerous to excise it.

Maclean³⁵ described a method which possesses merit. The duodenum is opened directly on its anterior surface in the descending portion. The neck of the sac is found and its relations to the ampulla visualized. The surgeon inserts his finger into the sac through its neck. It is then

TABLE I

DIVERTICULA DUODENUM, DESCENDING LOOP, SECOND PORTION, NO INFLAMMATION

| YEAR | AUTHOR | SEX | AGE | OPERATION | RESULT |
|------|------------------------|--------|-----|--|---|
| 1915 | Forsell and Key | Female | 41 | Resection, suture | Well |
| 1919 | Siegrist | Male | 48 | Resection, suture; adherent to pancreas | Well |
| 1925 | Lecene | Female | 52 | Resection, suture | Well |
| 1926 | Stiles* | | | Resection, suture | Well |
| 1926 | Kinard and Vandel | Male | 68 | Appendectomy; resection, suture | Well |
| 1926 | Grégoire | Female | 60 | Resection, suture | Well |
| 1929 | McQuay | | | | |
| | Case 3 | Female | 34 | Resection, suture | No change |
| | Case 6 | Female | 40 | Resection from pancreas; suture; degastroenterostomy | Well |
| 1931 | v. Friedrich | Male | 57 | Resection, suture | Not stated |
| 1932 | Hanke | | | | |
| | Case 2 | Female | 48 | Resection, suture | Symptoms re- curred |
| | Case 3 | Female | 43 | Posterior gastroenterostomy; diverticulum not disturbed | Well |
| 1932 | Harris | Female | 49 | Resection, suture; stone in diverticulum | Well |
| 1933 | Sullivan† | | | | |
| | Case 1 | Female | 56 | Resection from pancreas, suture | Local pancre- atic abscess draining |
| | Case 2 | Male | 63 | Diverticulum inverted; pylor- ectomy posterior gastro- enterostomy | Well |
| 1934 | Edwards | Female | 54 | Resection, suture | Well |
| 1936 | Tanner | Female | 65 | Resection from pancreas, suture | Well |
| 1936 | Fletcher and Castleden | | | | |
| | Case 1 | Female | 64 | Resection, suture | Well |
| | Case 2 | Female | 52 | Resection, suture | Well |
| | Case 3 | Female | 42 | Resection, suture; adherent to pancreas | Well |
| 1936 | Albers | Female | 40 | Resection, suture; chole- cystectomy for gallstones | Well |
| 1938 | Mendillo and Koufman | Male | 49 | Resection, suture; leiomyo- sarcoma in sac | Well |
| 1939 | Hellner | Female | 28 | Resection, suture | Well |

*See Spriggs and Marxer.

†See Barnes.

TABLE II

DIVERTICULA DUODENUM, THIRD PORTION, NO INFLAMMATION

| YEAR | AUTHOR | SEX | AGE | OPERATION | RESULT |
|------|------------------------|--------|-----|---|--------|
| 1917 | Basch | Female | 36 | Through mesocolon; resection, suture, posterior gastroenterostomy | Well |
| 1922 | Downes Case 2 | Female | 53 | Through mesocolon; resection, suture | Well |
| 1927 | Maclea Case 4 | Female | ? | Resection, suture | Well |
| 1927 | Jacquelin and Quénu | Male | 57 | Through mesocolon; resection, suture | Well |
| 1938 | Guthrie and Brown | Female | 50 | Resection, suture; degastroenterostomy | Well |

easy to dissect it from the surrounding tissues. The diverticulum is inverted into the duodenum. Its neck is ligated and it is removed. The opening in the anterior duodenal wall is repaired by suturing it in a transverse direction. This method is especially useful when the diverticulum is embedded in the pancreas.

When the diverticulum is in the third or fourth portion of the duodenum, it is still relatively inaccessible. It can be demonstrated by approaching this part of the duodenum through the transverse

TABLE III

DIVERTICULA DUODENUM, FOURTH PORTION, NO INFLAMMATION

| YEAR | AUTHOR | SEX | AGE | OPERATION | RESULT |
|------|------------------------|--------|-----|--|--|
| 1922 | Robineau and Gally | Female | 39 | Through mesocolon; resection, suture; attached to pancreas | Well |
| 1927 | Larimore and Graham | Female | 63 | Through mesocolon; had to cut Treitz ligament; resection, suture | Died, streptococcal peritonitis; no leak |
| 1927 | Maclea Case 3 | Male | 37 | Through mesocolon behind pancreas; resection, suture | No follow-up |
| 1927 | Krogius | Female | 64 | Through mesocolon; adhesions to jejunum; resection, suture | Well |
| 1928 | Lund | Female | 63 | Through mesocolon; resection, suture; accessory pancreas present | Well |
| 1933 | Denis | Female | 60 | Through mesocolon; resection, suture | No follow-up |
| 1933 | Cromie | Female | 38 | Through mesocolon; resection, suture | Well |
| 1933 | Barnes | Female | 58 | Through mesocolon; resection, suture | Well |
| 1936 | Christidi | Male | 32 | Through mesocolon; resection, suture | Well |

mesocolon. The retroperitoneal tissues are then divided. The duodenum is exposed from its under surface. The diverticulum is usually behind it and between the duodenum and the pancreas. Or it may be in the pancreas itself or behind this organ. It may be necessary to divide Treitz's ligament in order to get complete exposure.

In every case of diverticulum of the duodenum at operation a thorough investigation of the abdominal organs should be carried out. There is always a possibility that the symptoms are due to some associated pathologic lesion, the diverticulum being an incidental discovery.

Results from surgery of the duodenal diverticula are good as reported in the literature. Relief had been obtained in 80 per cent of the cases reviewed. In 8 per cent no follow-up was given; in 6 per cent the symptoms were not relieved. In one patient following operative removal a localized pancreatic abscess formed and was still draining at the time of the report. Drainage was used in 12 per cent, but these include the acute diverticulitis cases where it was indicated. In the uncomplicated resection there is no need for drainage unless the tissues have been severely damaged in the operation. Death occurred in 6 per cent. In two of these there were acute perforations; in the third, a streptococcus peritonitis.

Tables I-V were made up from articles consulted in the preparation of this report. There may be other contributions which have been overlooked, as not every reference could be followed up. Many diverticula associated with duodenal ulcer were eliminated as these represent secondary diverticula of the traction type. There were also

TABLE IV
DIVERTICULA DUODENUM, MULTIPLE, NO INFLAMMATION

| YEAR | AUTHOR | SEX | AGE | OPERATION | RESULT | SITE |
|------|-----------------------------------|--------|-----|---|--------|---|
| 1920 | Clairmont and Schinz Case 2 | Male | 36 | Excision with wall; transverse suture | Well | 2 diverticula in third portion |
| 1922 | Downes Case 3 | Female | 39 | Through mesocolon; could not find; then mobilized de- scending duode- num; resection, suture | Well | 2 diverticula in third portion |
| 1928 | Heidecker | Male | 54 | Inverted | Well | Multiple in duode- num and jejunum |
| 1929 | McQuay Case 10 | Female | 78 | Duodenotomy; re- section, suture; retraction of mes- ocolon; resection, suture | Well | 1 diverticulum in second portion, head pancreas 1 diverticulum in third portion |
| 1932 | Hanke Case 1 | Female | 43 | Resection, suture | Well | 3 diverticula in sec- ond portion |

TABLE V
DIVERTICULA DUODENUM, INFECTION, ACUTE AND CHRONIC

| YEAR | AUTHOR | SEX | AGE | SITE | OPERATION | PATHOLOGY | RESULT |
|--------|----------------------------|--------|-----|----------------------|--|---|--------|
| 1920 | Moore | Male | 58 | Descending loop (II) | Resection, posterior gastro-enterostomy | True diverticulum; moderate chronic inflammation | Well |
| 1923 | Maclean | Female | 58 | Desc. loop (II) | Duodenotomy, resection; diverticulum, drainage | Chronic pancreatitis | Well |
| 1923 | Huddy | Female | 27 | Desc. loop (II) | Resection, drainage | Gangrenous pouch; edema, retro-peritoneal tissues | Well |
| 1925 | Butler and Ritvo Case 1 | Male | 40 | Junction (I and II) | Inverted; reinforced | Markedly inflamed diverticulum | Well |
| 1926-7 | Monsarrat | Female | 58 | Desc. loop (II) | Resection, drainage | Perforated diverticula, <i>B. coli</i> abscess | Well |
| 1930 | Lucinian | Female | 36 | Desc. loop (II) | Resection | Perforation into head pancreas walled off inflamed reaction | Well |
| 1933 | Costello Case 1 | Male | 37 | Jet. (II and III) | Inverted | Marked peridiverticulitis | Well |
| 1938 | Beaver | Male | 54 | Desc. loop (II) | Abdomen drained; diverticulum not found at operation | Acutely inflamed diverticulum; ruptured apex into head pancreas | Died |
| 1939 | Boland | Male | 59 | Desc. loop (II) | Appendectomy; cholecystectomy | Perforated diverticulum; abscess head pancreas | Died |

a large number of excellent reviews on the diagnosis, pathology, and x-ray appearances of these diverticula. These have not been included in the bibliography as they made no contribution to the surgical treatment.

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THE PROBLEM OF SURGICAL ARREST OF MASSIVE HEMORRHAGE IN DUODENAL ULCER*

THE TECHNIQUE OF CLOSING THE DUODENUM

OWEN H. WANGENSTEEN, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

SURGEONS and internists alike, interested in and concerned with the vagaries of ulcer, have related that they have not had occasion to resort to direct surgical means for the arrest of massive hemorrhage in bleeding ulcer (Bier,⁷ Hurst and Ryle,¹⁷ Krönlein¹⁸). Up until quite recently this seemed to be almost universal experience; namely, that bleeding from an ulcer could be controlled by conservative means in almost all cases. For many years, however, Finsterer,^{8, 9} of Vienna, has been insisting that, if bleeding continued beyond forty-eight hours, recourse should be had to surgery. In this country, Allen, of Boston, was the first to insist on a program of direct operative attack for threatening bleeding. Since these expressions have appeared, many clinics have taken occasion to study their own experience with reference to massive bleeding (Hinton,^{15, 16} Pfeiffer,^{23, 24} Snell²⁶). Whereas previously it was believed on every hand and stated frequently that death from hemorrhage was a rare occurrence in ulcer, it is becoming more and more apparent that the lives of a fairly large number of patients with ulcer are lost through the agency of hemorrhage.

At the Municipal Hospital in San Francisco, Goldman^{11, 12} found that of 349 patients admitted because of gross hemorrhage 31 (11.1 per cent) died of exsanguination, while an additional 17 (4.9 per cent) died of complications initiated by bleeding. La Due¹⁹ reported the experience of the Minneapolis General Hospital, noting that 8 of 82 patients with bleeding ulcer died, a mortality of 9.8 per cent. Bergh, Hay and Traeh⁶ have summarized the experience of the Minnesota University Hospital, observing that 10 per cent of 70 patients treated conservatively for massive hemorrhage from ulcer died. In 2,565 collected cases of massive hemorrhage from ulcer treated conservatively, they found the mortality to be 10.2 per cent.

INDICATIONS FOR OPERATION

It is to be remembered that it was a long time after McBurney²⁰ first emphasized the necessity for early operation in acute appendicitis that surgeons began to have the opportunity of removing the

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appendix before it was ruptured. The fallacy of the widely-held belief that patients with ulcer die rarely of hemorrhage has just been exposed. Finsterer's dictum of operation if bleeding continues after forty-eight hours of conservative treatment is not likely to be put into immediate effect in a large number of medical and surgical clinics in this country. Both internists and surgeons are aware of the magnitude of the operative procedure necessary to arrest bleeding. At the same time, they know that in a certain number of instances bleeding will cease spontaneously. Further, both internists and surgeons wish objective proof that those who attempt the surgical arrest of hemorrhage from bleeding ulcer are able to carry such procedures through with a reasonable mortality.

A clearer definition of the indications for operative intervention is urgently needed. Meulengracht,²¹ who puts much emphasis on the value of frequent feedings to diminish the hazards of bleeding, admits having allowed nine patients to die of hemorrhage without submitting any to the surgeon. Following the example of Andresen⁴ (1927) a number of American internists have fed ulcer patients with bleeding ulcer frequently (La Due¹⁹), but without the same degree of success reported by Meulengracht. Patients suffering from massive hemorrhage are often too ill to eat and attempts at feeding with a duodenal tube succeed frequently in ascertaining that gastric stasis is present. In such instances, during the trial period, when it is being determined whether operation should be done, it is the custom in this clinic to apply suction to an indwelling tube. By this means, hydrochloric acid, the agent which activates the bleeding, may be removed about as effectually as it is neutralized by the ingestion of food, with the additional advantage that the nausea of gastric stasis is obviated. Gordon-Taylor,^{13, 14} who has had a large experience with the operative management of massive hemorrhage from ulcer, states that bleeding continuing after seventy-two hours of conservative treatment carries a risk of 78 per cent.

SIGNIFICANCE OF SHOCK

When an ulcer bleeds, blood may be lost slowly and gradually or quickly, depending on the size of the vessel that is eroded. In the instances of bleeding duodenal ulcer reported herewith that were subjected to operative intervention, an opening in the gastroduodenal artery was the uniform finding in those instances in which repeated bleeding to shock levels occurred. In other words, the craterous ulcer on the posterior duodenal wall had eroded through the duodenal wall completely. Perforation onto the gastroduodenal artery, which overlies the pancreas at this position, was the usual finding at operation. The artery, in turn, was eroded by the hydrochloric acid of the gastric juice with ensuing hemorrhage.

The significance of the occurrence of shock in bleeding ulcer cannot be emphasized too strongly. In all patients in whom it is difficult to sustain a satisfactory blood pressure, despite transfusion, it is apparent that blood is being constantly lost through a fairly large opening. Such patients in my opinion should be subjected early to operation. By choice, I would transfuse such patients and prepare for immediate operation. It is only fair to say, however, that, whereas such is my thought upon the matter, as a matter of fact, the patient reported here who was submitted earliest to operation after the onset of hemorrhage had bled for ninety-six hours (Case 1). In the other six patients of the series the time interval between onset of bleeding and operative intervention was twenty-four, twenty-three, eleven, twenty, eight, and seventeen days, respectively.

It is obvious that in all clinics where such operations are undertaken, internist and surgeon together must go through a proving period, during which time both become better acquainted with the limitations and advantages of conservative and operative management.

It must not be forgotten in patients transfused repeatedly for bleeding and in whom a second, third, or fourth episode of bleeding occurs that mere replacement of blood loss fails to afford the surgeon a patient well fortified to withstand the exigencies of a formidable operative procedure. Hemorrhage and depression of arterial pressure initiate a set of physiologic upsets that the administration of fluid and blood does not repair at once. This lag, exhibited by therapeutic procedures in catching up with the disturbed mechanisms which they are intended to relieve, must be appreciated more fully both by internist and surgeon. A patient who has bled to a critical level of blood pressure but once, granted immediate and full restoration of blood loss, is undoubtedly in a better position to withstand operation than the patient who has bled to shock levels repeatedly.

In the patient whose ulcer bleeds slowly but without the blood pressure falling to shock levels, the necessity for operation is not so urgent. Yet, the importance of not delaying too long is to be heeded here, too. It is significant that Finsterer^a is able to report a mortality of 5 per cent in those patients submitted to operation within forty-eight hours of the onset of hemorrhage. In the group operated upon after the elapse of longer intervals the mortality was 30 per cent.

AGE

In the literature one gathers the impression that it is only the patient over 50 years of age who is likely to bleed. In the group of patients with massive hemorrhage reported here, there was one 24 years of age (Table I, Case 2) and one 36 years of age (Case 4). The oldest patient in the group was 80 years old. Fatal bleeding from a duodenal ulcer in the newborn has been reported. It is obvious, there-

fore, that young patients with flexible arteries may bleed briskly or die of hemorrhage and that youth alone does not constitute assurance that bleeding will stop without operation. In other conditions in which openings in arteries exist, one does not hear that only the patient with an arteriosclerotic vessel runs a big risk of dying of exsanguination.

OPERATION

Two of the patients in the present group were subjected to preliminary gastroenterostomy because of pyloric obstruction associated with the bleeding. In one instance (Case 1) a direct attack upon the bleeding point became necessary five weeks later; in the other case (Case 2) division of the duodenum and gastric resection was undertaken seven days later because of recurrence of bleeding which threatened life. The futility of gastroenterostomy to relieve massive bleeding from ulcer should be regarded as established.

In the patients reported here, a direct attack has been made on the bleeding point. Steep Trendelenburg position with transfusions of large quantities of blood prior to and during operative procedure have been employed regularly. Cyclopropane has been the anesthetic agent, administered usually through an intratracheal tube. The operative approach has been made through a long right rectus incision.

OPERATIVE FINDINGS

In a bleeding duodenal ulcer it is surprising how minimal the obvious operative findings are on opening the peritoneal cavity. The presence of blood in the intestine and colon is readily apparent. The anterior duodenal wall and the stomach may appear normal. In none of the cases reported here was it definitely established prior to operation by x-ray examination that the patient had a duodenal ulcer, though in a few of the patients such a diagnosis had been established at an earlier date. As a matter of fact, not uncommonly it is only by efforts directed at separating the medial wall of the duodenum from the pancreas that the presence of a hemorrhagic lesion is established definitely. When the duodenum is opened, by uncovering the perforation the gastroduodenal artery with a slit or a hole in its wall from which blood escapes in jets is visualized at the base of the ulcer crater.

Statistically, a number of studies (Allen,² Snell²⁶) have determined that a bleeding duodenal ulcer is the most likely cause of massive hemorrhage. If, therefore, the medial wall of the duodenum is applied closely to the adjacent pancreas, the possibility of a small craterous ulcer on the posterior duodenal wall being responsible for the hemorrhage is likely. Such an ulcer may not even be felt and, of course, cannot be seen as long as the duodenum remains in contact with the pancreas. This occurrence, which has come repeatedly now to my attention, suggests that a number of patients who have melena of unlo-

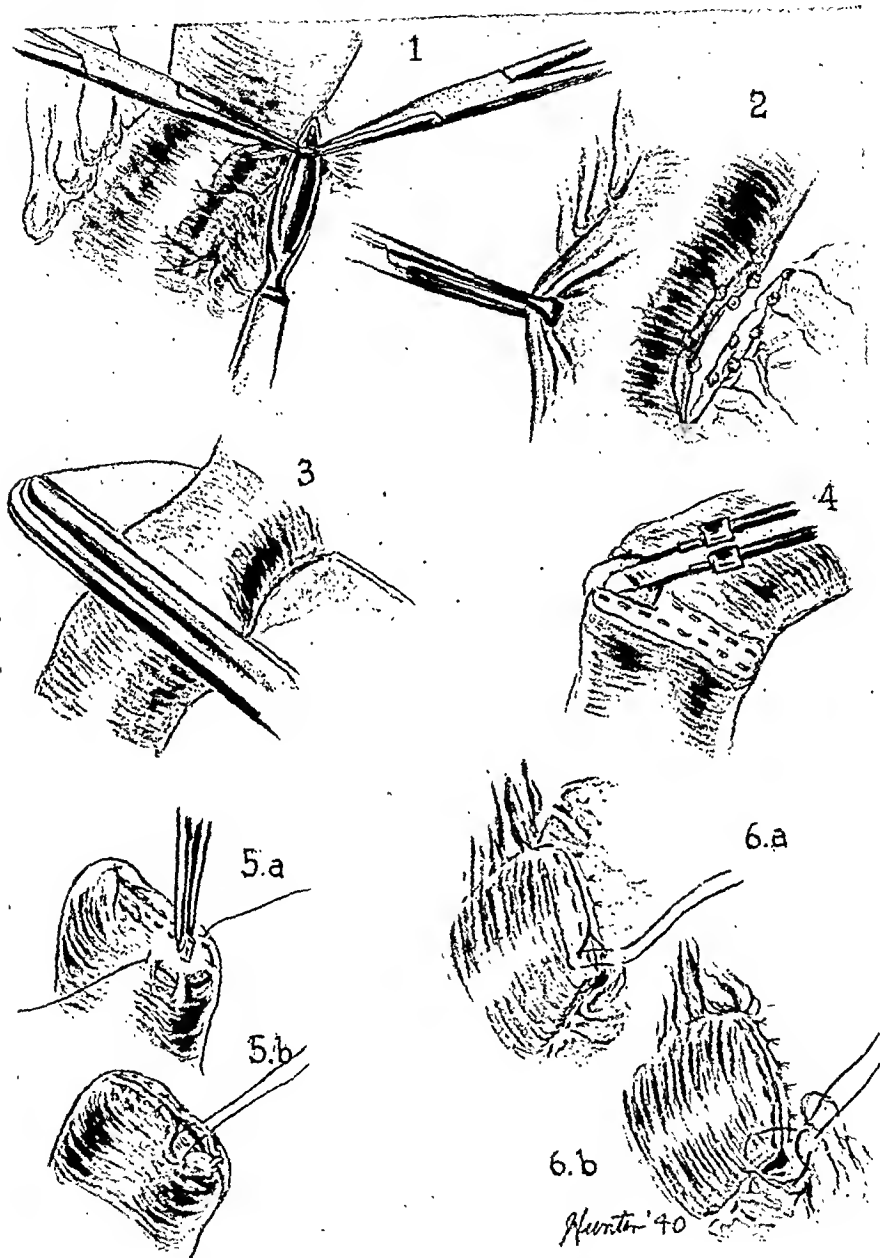


Fig. 1.—Dissection for closure and inversion of duodenum in the Billroth II type of operation. This is the method I employ when the duodenal wall is intact. This method, obviously, is not applicable for duodenal closure when the posterior duodenal wall is perforated.

The attachment between pancreas and medial (posterior) wall of the duodenum is separated as indicated in 1. The detachment is adequate to permit satisfactory inversion as indicated in 2. In 3 is shown application of the Petz clamp. Division with the cautery is shown in 4. 5a indicates the manner of inverting the duodenal ends and 5b the closure obtained with a single row of interrupted sutures of fine silk placed after the Halsted mattress pattern. In 6a is shown the manner of reattaching the pancreatic capsule to the anterior duodenal wall. The manner of placement of sutures at the ends shown in 6b assures a closed space on the posterior aspect of the duodenal wall.

This method of dissection and suture provides a satisfactory means of securing safe closure of the duodenum.

calized origin may have such an ulcer, which may have escaped detection even by x-ray examination. Such instances have come to my notice. An occult posterior wall duodenal ulcer should be considered in cases of gastrointestinal hemorrhage where the cause remains obscure.

If the posterior duodenal wall is not applied closely to the pancreas and if its wall may be separated from the pancreas with a dissector, it is apparent that it is not the source of bleeding. Whereas induration of the anterior duodenal wall has been present as a concomitant finding in a few of these cases, I have not observed brisk bleeding from an ulcer on the anterior duodenal wall. If examination of the posterior duodenal wall shows it to be removed from immediate contact with the pancreas, search should be extended to the stomach, to the stoma if an antecedent gastroenterostomy has been made, and to a Meckel's diverticulum. I have observed sharp hemorrhage from a gastrojejunal ulcer (Case 7) when no ulcer could be palpated at the stoma from without. *In instances in which the stomach cannot be dismissed as a source of bleeding, when other likely origins of the hemorrhage can be excluded reasonably (posterior duodenal wall ulcer and Meckel's diverticulum), an incision transverse to its axis should be made in the body of the stomach. With employment of appropriate deep-bladed retractors, after sponging, the bleeding point will be located if it has its origin within the stomach.*

ARREST OF HEMORRHAGE IN DUODENAL ULCER

Having determined by dissection that perforation of the posterior wall of the duodenum onto the pancreas has occurred, the opening in the duodenal wall is extended around the entire circumference of the bowel. This maneuver affords quick exposure of the bleeding point and the objective of the operative procedure; namely, adequate arrest of hemorrhage may be attained within a few minutes after the abdomen is opened. Thereafter, the difficult closure of the duodenal stump and the establishment of a gastrointestinal anastomosis after gastric resection may be undertaken leisurely.

CLOSURE OF THE DUODENAL STUMP

Closure of the blind end of the duodenal stump in the ordinary gastric resection is accomplished easily and is illustrated in Fig. 1. After separating the pancreas adequately from the bowel wall, the duodenum is sectioned between Petz clips with the cautery. A single row of Halsted mattress sutures of fine silk affords usually a satisfactory closure. When, however, the posterior duodenal wall has perforated, satisfactory closure of the duodenum is a most difficult procedure. In the first two patients operated upon in this series, a metal probe was placed in the ampulla of the choledochus while the

bowel wall was being sutured up. One of the deaths in the group (Case 4) was a technical failure, owing to insecure closure of the duodenal stump, with resultant leakage. In this instance the perforation constituted a veritable large granuloma in the medial duodenal wall posteriorly.

When the bleeding vessel has been ligated securely, the posterior duodenal wall is separated adequately from the pancreas to permit closure of the open duodenum as indicated in Fig. 2. This necessitates usually complete excision of the ulcer. In the main it is not possible to mobilize the duodenal wall to secure the type of duodenal wall closure illustrated in Fig. 1. On the contrary, one must be satisfied with burying the closed duodenum in the anterior wall of the pancreas. Attending perforation of the duodenal wall, thickening of the pancreatic capsule occurs, making it practicable to employ it as an additional safeguard to secure effectual closure of the duodenum. This is the only feature of the operation that requires special comment. The technical aspects of the problem are depicted well in the drawing made for me by Mr. Herbert Hunter. In the absence of hemorrhage Finsterer⁸ and others who practice extensive gastric resection with antral exclusion for the treatment of duodenal ulcer are content to regard the ulcer in the duodenum, presenting the technical difficulties described here, as irremovable. Finsterer admits freely that the difficulties involved in securing an effectual closure of the duodenum after excision of the ulcer, pyramids the mortality, as contrasted with leaving the ulcer. However, in the presence of active massive hemorrhage there is no choice. In my experience the most satisfactory manner of arresting the bleeding is to open the duodenum as described above, ligating the bleeding vessel or excising the ulcer by placement of sutures. Nissen²² and Gohrbandt¹⁰ have described closure of the duodenum after excision of "irremovable duodenal ulcer" by techniques very similar to those I have employed.

The operation is completed by excising the antrum and a good portion of the acid-secreting area of the stomach to minimize further trouble from the acid ulcer diathesis. The objective of well-directed surgery in the management of ulcer should be to secure a stomach which empties rapidly and which is achlorhydric to maximal stimulation (histamine). This anastomosis I establish by the closed or aseptic method, the details of which have been described previously (Fig. 3). Unless a gastroenterostomy has been made previously, delimiting the proximal extent of the resection, an attempt should be made to excise a generous segment of the corporic and fundic zones to insure effectual reduction of gastric acidity. After the hemorrhage has been satisfactorily controlled, such adequate excision of gastric tissue adds but little to the risk, but has important significance for the ultimate results.

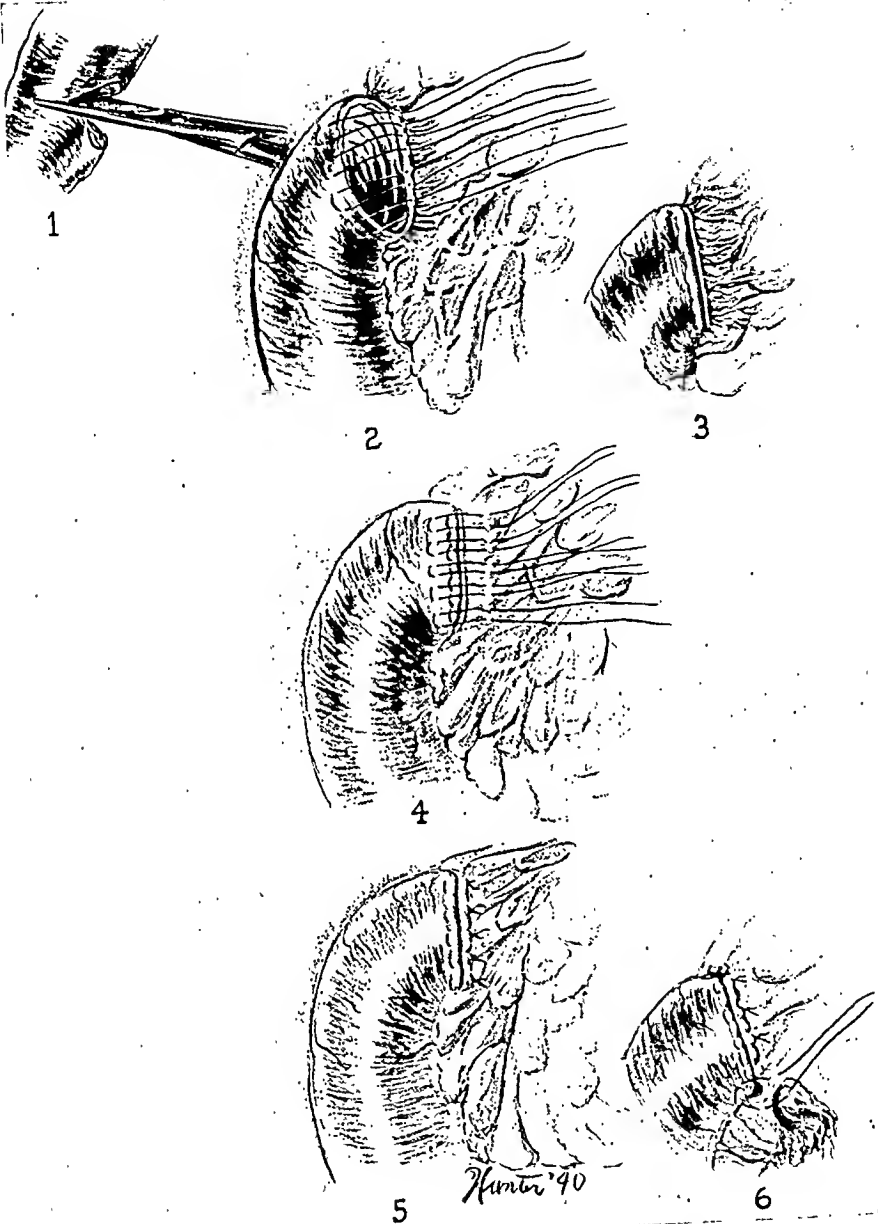


Fig. 2.—Method of closure of duodenum in massive hemorrhage causing shock and necessitating emergency operation for arrest of bleeding. Such an ulcer presents invariably perforation on the posterior duodenal wall and the technique depicted in Fig. 1 cannot be employed.

The dissection and separation of the medial (posterior) duodenal wall from the pancreas is begun as shown in the first step in Fig. 1. This dissection succeeds in disclosing a perforation in the posterior duodenal wall in massive hemorrhage. The anterior duodenal wall is then cut across totally with scissors as indicated in 1 and the bleeding vessel is ligated.

In 2 is shown the placement of interrupted Halsted mattress sutures of fine silk across the open end of the duodenum. None are tied till all are placed. The duodenal walls are approximated as shown in 3 when the sutures are tied. This closure is by no means as satisfactory as that shown in 5a and 5b in Fig. 1, employed when the duodenal wall is not perforated. However, when reinforced as shown in 4, 5, and 6 there by burying the closed duodenal end in the pancreatic capsule, a satisfactory closure usually can be obtained even in difficult cases. Particular note is to be taken of the manner of insuring a closed space on the posterior duodenal wall (6). This is a most important item in the procedure. Such a suture is placed at the upper end as well.

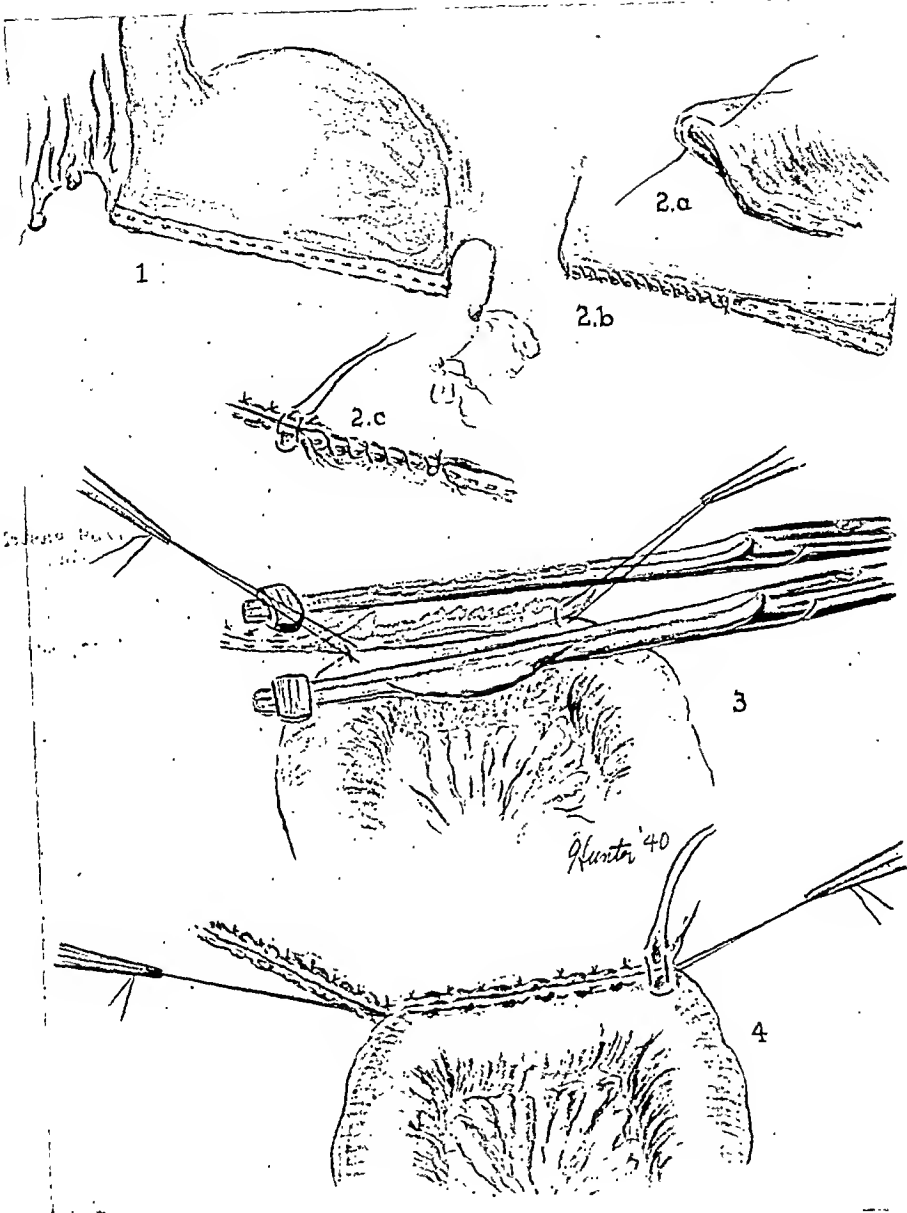


Fig. 3.—Aseptic gastric resection, method of establishing gastrointestinal continuity. The aseptic or closed method was employed in all the cases listed herein (Table I). In the first six cases excision of the pylorus and antrum only was done (complete termino-lateral anastomosis [Polya]) without enteroanastomosis. In Case 7 the excision was of the extent shown here and an incomplete (inferior) terminolateral (Hofmeister) anastomosis with enteroanastomosis was made, the type of excision and anastomosis carried out as an elective procedure for complicated ulcer when the Billroth II method is employed. Achlorhydria even to maximal stimulation with histamine follows this extent of excision of gastric tissue usually; achlorhydria attends antral excision rarely. In 1 is shown the site of amputation of the stomach and the clips deposited by the Petz suturing apparatus. 2a indicates the manner of inversion of the dog ear at the upper end. The dotted line at the lower end of the stomach in 2b indicates the site at which the anastomosis will be established. This small segment of stomach is removed with the cauterizer after satisfactory hemostasis has been attained by a running suture of catgut over the Petz clips where the stomach is inverted above. The inversion is obtained with a single row of fine silk sutures placed after the Halsted mattress pattern (2c). In 3 is indicated the manner in which the anastomosis (6 cm. in length) is established by the closed or aseptic method. It is to be noted that the portion of the jejunum engaged in the clamp is not cut off until the posterior row of sutures has been placed. In 4 the completed anastomosis is shown. The details of this technique have been described previously.

TABLE
OPERATIONS FOR MASSIVE HEMOR

| CASE NO. NAME HOSPITAL NO. AGE | OPERATIVE DIAGNOSIS | DURATION OF BLEEDING | PREVIOUS OPER- ATIVE PROCEDURE | OPERATION*— DATE, PRO- CEDURE, SIZE OF RESECTION | DURATION OF OPERATION |
|---|--|----------------------------|---|--|------------------------------------|
| 1. Mr. C. M. No. 623906 49 yr. | Perforated posterior wall duodenal ulcer with erosion of gas- troduodenal artery | 96 hr. | 11/14/38 gastro- enterostomy for bleeding | 12/17/38 gastric resection | 1 hr. 50 min. |
| 2. Mr. L. K. No. 669044 24 yr. | Perforated posterior wall duodenal ulcer with erosion of gas- troduodenal artery | 24 days | 2/14/39 gastro- enterostomy for bleeding | 2/21/39 gastric resection 5/15/39 Schmil- insky operation | 1 hr. 55 min. 2 hr. 40 min. |
| 3. Mr. L. W. No. 643715 52 yr. | Perforated posterior wall duodenal ulcer with erosion of gas- troduodenal artery | 23 days | | 9/3/39 gastric resection | 2 hr. 35 min. |
| 4. Mr. G. C. No. 611604 36 yr. | Perforated posterior wall duodenal ulcer with erosion of gas- troduodenal artery | 11 days | | 9/17/39 gastric resection | 2 hr. 50 min. |
| 5. Mr. J. K. No. 669010 80 yr. | Perforated posterior wall duodenal ulcer with erosion of gas- troduodenal artery | 20 days | None | 9/17/39 gastric resection | 2 hr. 45 min. |
| 6. Mr. G. A. No. 661081 58 yr. | Perforated posterior wall duodenal ulcer with erosion of branches of gastro- duodenal artery | 8 days | None | 9/18/39 gastric resection | 2 hr. 55 min. |
| 7. Mrs. E. F. No. 693430 57 yr. | Duodenal ulcer with obstruction, with bleeding gastroje- junal ulcer | 17 days | 20 yr. ago gas- troenteros- tomy | 4/13/40 gastric resection | 3 hr. 30 min. |

*All gastric resections in the group are antral resections (pylorus and antrum) except Case 7, in which 75 per cent of the total square area was excised. Enterostomy was done in Case 7 only. Save for the patient in Case 3, who has occasionally been achlorhydric, only one of the survivors (Case 7) has been persistently achlorhydric to stimulation with histamine.

†All the survivors have reported for examination on several occasions since this was written. All are subjectively and objectively well.

In my experience the removal of 200 sq. cm. of gastric tissue (measured on the peritoneal surface) with a Polya type of anastomosis insures quite uniformly effectual reduction of gastric acidity. Scott found the average total square area of the gastric mucosa in six adult stomachs to be 525 sq. cm. Scott's measurements, however, took into account the rugation of the mucous folds. It is apparent, therefore, that more than 200 sq. cm. of gastric mucosa is sacrificed actually in the excision of gastric tissue described above. On the basis of a larger number of gastric resections done for other varieties of ulcer,

HEMORRHAGE FROM DUODENAL ULCER*

| IMMEDIATE RESULTS | ULTIMATE RESULTS† | AMOUNT OF BLOOD TRANSFUSED | LABORATORY | BLOOD PRESSURE (LOWEST JUST BEFORE OPERATION) | PULSE (HIGHEST JUST BEFORE OPERATION) |
|----------------------------|--|--|----------------------------|---|---------------------------------------|
| Recovered | 2/26/40 well | 1,100 c.c. before operation; 1,700 c.c. during operation; 300 c.c. after operation | Hb. 38 R.B.C. 2,500,000 | 76/58 shock | 110 |
| Recovered | 9/16/39 died from perforated jejunal ulcer | 3,500 c.c. before first; 4,750 c.c. before second, 500 c.c. after second, 1,500 c.c. after third operation | Hb. 32 R.B.C. 2,170,000 | 0/0 shock | Not palpable |
| Recovered | 4/22/40 well | 2,200 c.c. | Hb. 42 R.B.C. 2,480,000 | 82/54 shock | 112 |
| 9/19/39 died, peritonitis | | 4,000 c.c. | Hb. 47 R.B.C. 3,500,000 | 68/32 shock | 122 |
| Died 8 hr. after operation | | 500 c.c. | Hb. 55 R.B.C. 2,850,000 | 74/50 shock | 120 irregular |
| Recovered | 4/23/40 well | 1,000 c.c. before operation; 500 c.c. during operation; 500 c.c. right after operation; 1,500 c.c. after operation | Hb. 39 R.B.C. 2,400,000 | 120/82 No shock | 108 |
| Recovered | 4/25/40 discharged, well | 9,600 c.c., including 2,600 c.c. before and after operation (7,000 c.c. at Miller Hospital, St. Paul) | Hb. 30 | 64/32 shock | 136 |

I estimate that it is necessary to sacrifice two-thirds to four-fifths (66 to 80 per cent) of the total gastric area (in an unobstructed stomach of average size) to remove 200 sq. cm. measured as indicated above. Such resection, when accompanied by a gastrojejunal anastomosis, affords a stomach which is achlorhydric usually even to maximal stimulation. Similar extensive gastric resection, unaccompanied by gastrojejunostomy, fails to make the stomach achlorhydric.^{28, 29}

It is becoming recognized more generally that gastrointestinal surgery is a highly specialized variety of operative procedure. The two Mayos, to whom these pages are dedicated, established an enviable record in the management of gastric lesions. Balfour's accomplish-

ment with difficult gastric operations attests the importance of concentrating this type of surgery in the hands of a few persons in every surgical clinic.

IMPORTANCE OF ADEQUATE ARREST OF HEMORRHAGE

In Allen and Benedict's first group of fatal cases from massive hemorrhage, there were 28 patients. Twenty died under conservative management; 8 died after surgery; of these 8 cases, all but 1 died of hemorrhage. Ligature of the gastroduodenal and the right gastroepiploic arteries does not suffice to control hemorrhage. Bleeding may still occur through the open vessel in the base of the ulcer, via the inferior pancreaticoduodenal artery, a branch of the superior mesenteric.

In the present group there were 2 deaths. Neither died of hemorrhage. One (Case 4), aged 36 years, died two days after operation because of inadequate closure of the duodenal stump. The other, a man 80 years of age (Case 5), died eight hours after operation. His condition on the completion of the operation was better than at the beginning. I declined to operate because of the patient's age and poor condition twenty-four hours earlier and intervened in time to accept the lethal issue as a surgical death. Granted that the bleeding is arrested effectually, these patients, in the main, stand prolonged operation well (see Table I for time and length of operation). In all the patients listed here, operation was undertaken as an emergency operation for the control of hemorrhage. In most instances the operation could reasonably have been described as an ante-mortem operation.

My experience in the control of massive hemorrhage is outlined in Table I. There were 2 deaths among 7 cases, a mortality of 28.5 per cent.* The records of the hospital indicate that in 8 other instances, dating back to 1921 when the first case was done, operation has been undertaken for the control of active hemorrhage of ulcer origin. Three of the 8 died, a mortality in this latter group of 37.5 per cent. These operations, however, were largely indirect procedures.

SUMMARY

Massive hemorrhage is a not uncommon cause of death in duodenal ulcer. Approximately 10 per cent of patients treated conservatively for massive hemorrhage of ulcer origin die. The lives of a number of such patients may be salvaged by timely surgical intervention. The recovery of 5 of 7 patients subjected to ante-mortem operation for the control of hemorrhage suggests, in the main, that such patients stand

*Since this paper was written, three additional patients exhibiting massive hemorrhage from duodenal ulcer have been operated upon after the plan outlined in Fig. 3. All three recovered and have been observed in the out-patient clinic, and all are achlorhydric to histamine stimulation. (Mr. W. W., U.H. No. 647102, aged 67 years; Mr. P. S., U.H. No. 695376, aged 59 years; and Mr. L. A., U.H. No. 677349, aged 26 years.) The mortality in this group up to date, therefore, is 10 per cent.

operation tolerably well if the bleeding is adequately controlled. A means of uncovering the bleeding point, dealing with the open vessel, and a manner of securing satisfactory closure of the duodenum are described.

It is pointed out that fall of blood pressure to a shock level, necessitating transfusion of large quantities of blood to maintain the blood pressure at 100 mm. Hg, suggests that the patient has an open vessel. In massive hemorrhage from duodenal ulcer the gastroduodenal artery is eroded, owing to perforation of the posterior duodenal wall. The ulcer itself is often occult, presenting usually even at operation during active hemorrhage no tangible signs until the perforation is uncovered. Patients with duodenal ulcer who bleed slowly to low levels of hemoglobin (20 to 40) without manifesting significant falls in blood pressure do not exhibit complete perforation of the duodenal wall nor do they have a hole in a large vessel, but present usually erosion of small vessels within the bowel wall.

The most difficult question to decide is when operation should be undertaken. No one can say in which patients bleeding will cease automatically. The longer the bleeding period before operation, the more serious is the risk. The patient with massive hemorrhage who bleeds to shock level, in whom it is difficult to maintain a satisfactory blood pressure, should be submitted to immediate operation, as soon as blood loss is replaced adequately. In other patients Finsterer's dictum of waiting forty-eight hours to determine whether bleeding will cease spontaneously is sound advice. However, until the hazards of massive hemorrhage become known more generally, it is not likely that patients with threatening hemorrhage will come to operation early.

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THE USE OF THE MILLER-ABBOTT TUBE IN THE SURGERY OF THE LARGE BOWEL

ALLEN O. WHIPPLE, M.D., NEW YORK, N. Y.

(From the Department of Surgery, Columbia University, and the Presbyterian Hospital)

DURING the past decade one of the most remarkable advances in surgical therapy has occurred in the treatment of the ever-dreaded lesion of acute ileus. In 1918 the mortality in this condition, in three of the leading university clinics of this country, was 66 per cent. Following the better understanding of fluid and electrolyte imbalance,¹ so striking in cases of high intestinal obstruction, and the application of this knowledge in restoring this balance before operation, the mortality showed an amazing decrease. In the Presbyterian Hospital in New York City the mortality dropped from the figure of 66 per cent in the 1919 to 1924 period to 29.6 per cent in the 1932 to 1937 period.² This improvement was due chiefly to restoration of fluid and salt balance, but a considerable credit was also due to the use of continuous duodenal suction, before and after operation, by the method popularized by Wangensteen's³ classic work.

Following extensive experimental studies in intestinal intubation by Miller and Abbott⁴ and their associates, Abbott applied the technique to the management of clinical cases of intestinal obstruction. The first sixteen cases so treated were reported by Abbott and Johnston⁵ in 1938. Abbott,⁶ in Philadelphia, and Johnston⁷ and his co-workers, in Detroit, have continued the work in a large number of cases with amazing success.

Following Abbott's first report, we became convinced of the possibilities of this method in treating acute ileus and in 1938 we assigned two of our residents to this study. After observing the technique by Abbott, in Philadelphia, Leigh and Nelson of our surgical staff and Swenson of our roentgenological staff studied every case of acute ileus, mechanical and paralytic, in the Presbyterian Hospital. In 1939 we assigned one of our head nurses, Miss Stines, to the care of these patients as regards the detailed management and care of the tubes, and she has worked with the residents in this important field.

Our results in cases of acute ileus, using the Miller-Abbott intubation, have been so dramatic that we hesitated to report them; but, following almost equally striking results by Johnston and his associates in Detroit, Leigh, Nelson and Swenson⁸ reported our results in February of this year. The summary of this report is taken from their paper and is given in Table I. In addition to intubation these patients all had

analyses of their blood structure and fluid and salt balance restoration, which accounts for some of the remarkable improvement in the mortality of acute ileus.

It is important to emphasize the fact that this method of intestinal intubation carries with it tremendous possibilities for good as well as danger to the patient, depending upon the thorough understanding of these possibilities and the intelligent and diligent application of the technique of the method. The reason that so many hospitals have failed to appreciate the value of the Miller-Abbott tube in dealing with cases of ileus is that no one person has learned the application and technique of the method and acquired the experience necessary to its success. The reader is referred to the paper by Leigh, Nelson, and Swenson⁸ for a detailed discussion of the proper use of the tube in intubating the intestine.

TABLE I

SUMMARY OF CASES OF SMALL INTESTINAL OBSTRUCTION TREATED WITH MILLER-ABBOTT TUBE AND SURGERY

| TYPE OF OBSTRUCTION | NO. OF CASES | OPERATIONS FOR ILEUS | DIED | MORTALITY |
|--|--------------|----------------------|------|-----------|
| Noninflammatory obstructions | 50* | 27 | 1 | 2.0% |
| Paralytic type | 12 | 1 | 0 | 0 |
| Mechanical type | 38 | 26 | 1 | 2.7% |
| Obstructions with peritonitis | 21 | 10 | 7 | 33.3% |
| Tube passed into small bowel | 14 | 2 | 1 | 7.1% |
| Tube failed to pass into small bowel | 7 | 8† | 6 | 85.7% |
| Obstructions with gangrene of bowel | 5 | 6† | 2 | 40.0% |
| Total cases with obstruction | 76 | 43 | 10 | 13.2% |
| Total cases with tube passing into small bowel | 68 | 35 | 4 | 5.9% |

*One case discontinued. Patient hysterical.

†Two cases required two operations for ileus.

As these studies in acute ileus progressed, we appreciated the possibilities of using the Miller-Abbott tube as a preoperative measure to prevent distention and vomiting after intestinal resection. In peritonitis cases we had learned of the possibilities of feeding patients wearing the tube and the possibilities of restoring protein and vitamin loss in depleted patients. We believe the most important single factor in the success of intestinal anastomosis is to avoid distention of the anastomosed segment. Distention favors tension on the suture line and diminishes the blood supply in the gut wall, resulting in devitalization of the tissues included in the sutures, separation of agglutinated edges, leakage of gas and intestinal contents, with peritonitis or at best a fistula with localized peritonitis. For small intestinal anastomosis and for one-stage right-sided colectomy with ileocolostomy the advantages of a collapsed normal bowel before and after operation were obvious, and our results with the pre- and postoperative use of the tube clearly corroborated

TABLE II
MORTALITY OF RESECTIONS OF LARGE BOWEL (112 CONSECUTIVE CASES—1938-1940)*

| | WITHOUT MILLER-ABBOTT TUBE | | | MILLER-ABBOTT TUBE USED IN PRE- AND POSTOPERATIVE PERIODS | | | | TOTALS | | |
|---|----------------------------|--------|-----------|---|--------|-----------|------------|--------|-----------|--|
| | RESECTIONS | DEATHS | MORTALITY | RESECTIONS | DEATHS | MORTALITY | RESECTIONS | DEATHS | MORTALITY | |
| Right colon, one stage | 7 | 1 | 14.3% | 15 | 0 | 0 | 22 | 1 | 4.5% | |
| Left colon, one stage | 15 | 3 | 20.0% | 5 | 0 | 0 | 20 | 3 | 15.0% | |
| Left colon, obstructive resections | 18 | 4 | 22.2% | 5 | 1 | 20.0% | 23 | 5 | 21.0% | |
| Rectosigmoid, one-stage abdominoperineal resections | 28 | 4 | 14.3% | 11 | 0 | 0 | 39 | 4 | 10.3% | |
| Rectosigmoid, two stage | 8 | 2 | 25.0% | 0 | 0 | 0 | 8 | 2 | 25.0% | |
| Totals | 76 | 14 | 18.4% | 36 | 1 | 2.8% | 112 | 15 | 13.4% | |

*Thirty-six cases with one death where Miller-Abbott tube was passed preoperatively and used postoperatively until normal bowel function was established. One death due to a lung abscess following a pulmonary infarction. No postoperative distention. Tube out second postoperative day, infarction eighth postoperative day, death twenty-first postoperative day.

this premise. When we tried the tube in cases of left-sided colectomy and abdominoperineal resections of the pelvic colon and rectum, we found that the results were not so striking. In fact cecostomy as a preliminary measure in these cases where mechanical obstruction was complete or nearly so is still clearly indicated, because the tube does not pass the ileocecal valve in a distended cecum, and the additional pre- and postoperative use of the tube helps only in preventing postoperative ileus and distention of the small intestine, a very great boon in many of these cases, as regards their freedom from distention, vomiting, and tension on the abdominal wound.

TABLE III

CAUSES OF DEATH (112 CONSECUTIVE RESECTIONS OF LARGE BOWEL—1938-1940)*

| | RIGHT COLON | LEFT COLON | | ABD.-PER. RESECTIONS | | TOTALS |
|--|-------------|------------|------------------------|----------------------|-----------|--------|
| | ONE STAGE | ONE STAGE | OBSTRUCTIVE RESECTIONS | ONE STAGE | TWO STAGE | |
| <i>Directly related to operative procedure</i> | | | | | | |
| Peritonitis | 1 | 1 | 1 | 0 | 2 | 5 |
| Intestinal obstruction | 0 | 1 | 0 | 2 | 0 | 3 |
| Hemorrhage from perineal wound | 0 | 0 | 0 | 1 | 0 | 1 |
| <i>Indirectly related to operative procedure</i> | | | | | | |
| Pneumonia | 0 | 1 | 2 | 0 | 0 | 3 |
| Hemophilia—hemorrhage | 0 | 0 | 1 | 0 | 0 | 1 |
| Lung abscess | 0 | 0 | 1 | 0 | 0 | 1 |
| Cerebral hemorrhage | 0 | 0 | 0 | 1 | 0 | 1 |
| Totals | 1 | 3 | 5 | 4 | 2 | 15 |

*Peritonitis was always complicated by intestinal obstruction. Early peritonitis only in cases with abscess at operation. Late peritonitis followed wound infections or leakage of anastomosis.

We are reporting 112 consecutive unselected cases operated upon by our surgical staff during the years 1938-1940. Tables II and III give the results in the surgery of several parts of the colon (including rectum) with the one- and two-stage resections and the obstructive resections (Rankin operation), with and without the pre- and postoperative use of the Miller-Abbott tube and the total cases. The figures speak for themselves. We, at least, are convinced from the observation of our patients that the pre- and postoperative use of the tube in the surgery of the colon is not only a lifesaving measure, but one that adds greatly to the comfort and smooth convalescence of the patients undergoing this hazardous type of surgery.

We must again emphasize the absolute necessity of having some one member or members of the surgical staff learn the technique and management of intestinal intubation if it is to be used to treat or prevent

intestinal obstruction or distention, and again urge the careful reading of the previous communication from this clinic by Leigh, Nelson, and Swenson.⁸

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REGIONAL LYMPHATIC METASTASIS OF CARCINOMA OF THE RECTUM*

FREDERICK A. COLLIER, M.D., EARLE B. KAY, M.D., AND
ROBERT S. MACINTYRE, M.D., ANN ARBOR, MICH.

(From the Departments of Surgery and Pathology, University of Michigan)

A KNOWLEDGE of the lymphatic spread of carcinoma from primary lesions of the rectum is essential in the treatment of that disease. The normal lymphatic drainage of the rectum and rectosigmoid colon is well known, but it is often impossible to decide before operation whether metastasis has occurred or not. Consequently, we have no method of determining with certainty the operability and prognosis of any given carcinoma of the rectum.

The aim of the surgical treatment of carcinoma of the rectum is cure. The surgical procedure directed toward the removal of the primary tumor alone is of little value, other than perhaps temporary palliation. To effect a cure, both the primary neoplasm and its metastases must be excised. This is impossible in cases of hematogenous metastasis, but the regional lymph node metastasis frequently is amenable to operative removal.

This study, similar to one made by Gilchrist and David,¹ is based on the dissection and examination of all the lymph nodes from 53 carcinomas of the rectum. Of these, 48 were removed by combined abdominal-perineal resection, one by perineal resection, and four were autopsy specimens. The lymph nodes were dissected from each specimen after they had been visualized (Fig. 1) by clearing by the Spalteholz method as modified by Gilchrist and David. All nodes were examined individually and the results charted on previously prepared outline drawings upon which each node was indicated. These findings were then correlated with (1) the age of the patient, (2) duration of symptoms, (3) gross type of lesion, (4) location above the mucocutaneous junction, (5) site of origin of the neoplasm, (6) size, (7) amount of circumference of the bowel wall involved, (8) depth of infiltration, (9) microscopic type, (10) degree of cellular differentiation, and (11) the presence of associated precancerous lesions, such as polypi and ulcerative colitis.

Regional lymph nodes may thus be isolated which, because of their smallness, go unnoticed by the usual method of dissection. Specimens have been examined in which there were no nodes palpable but which, upon clearing, were found to include lymph nodes as small as 1 to 2 mm. in diameter, containing nests of metastatic carcinoma (Fig. 2). No correlation existed between the size of the lymph nodes and the

*This study was aided by the James and Elizabeth Inglis Fund for Surgery Research.

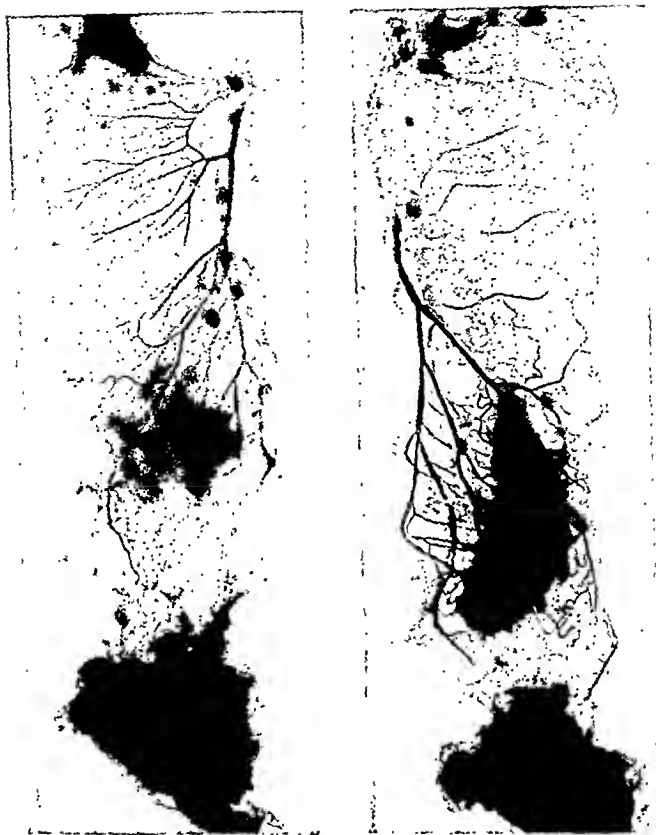


Fig. 1.—Photographs of cleared specimens of carcinomas of the rectum.

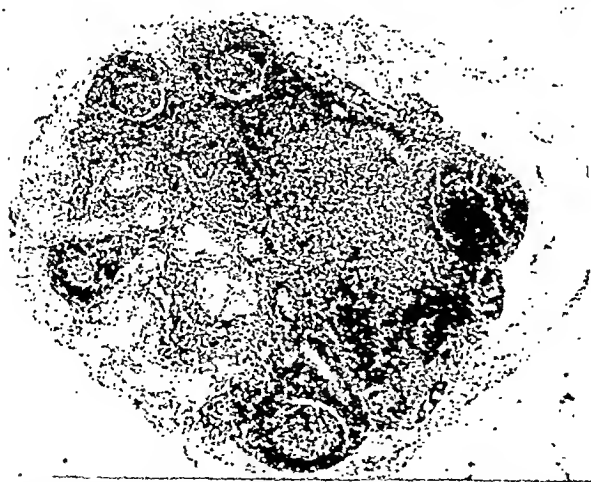


Fig. 2.—Photomicrograph of a lymph node only 1.5 mm. in diameter, showing meta-static carcinoma in the subcapsular lymph channels.

presence in them of metastases. Many large nodes were inflammatory and many small impalpable nodes contained neoplasm.

For comparison we studied a similar group of cases treated in 1934 and 1935. These specimens were examined by gross manual dissection and an average of only 3.5 lymph nodes per specimen were found. The largest number of nodes found by this method in any one specimen was 12, and 25 out of 46 cases (54 per cent) were reported as being free from metastases. In the present study as many as 194 lymph nodes have been isolated from a single operative specimen, and an average of 67 per specimen was found. With this more accurate method of study, the number of cases showing no involvement of the lymph nodes has decreased to 35.8 per cent. In other words, 64.2 per cent of the cases examined had metastases in the regional lymph nodes. This finding is similar to that of Gilchrist and David who found 68 per cent of the specimens to have metastases in the lymph nodes.

Regional lymph node metastasis is only one factor in determining the operability and prognosis in carcinoma of the rectum. Inoperability or poor prognosis may result from extensive local infiltration, hematogenous metastases, or peritoneal implants. In the most favorable of our cases, those in which radical operation was performed, 15 per cent showed microscopic evidence of infiltration into blood vessels. The hematogenous spread of carcinoma is an unpredictable factor. In one of our cases symptoms of occasional rectal bleeding had been present for only one month. The neoplasm, measuring only 2 cm. in diameter, had infiltrated just to the muscle layer and was a moderately well-differentiated adenocarcinoma mucosum of Grade II malignancy. Judged by clinical criteria, this patient had a good prognosis, but microscopic examination showed invasion of both lymph and blood vessels. The degree of malignancy was not a determining factor in the occurrence of hematogenous metastases, for, of the specimens in which metastasis was found microscopically, six lesions were Grade II, one was Grade IV, and one a spindle-cell sarcoma. Two of these had invasion of the blood vessels but no lymphogenous metastases.

According to the classic description of the lymphatic spread of carcinoma of the rectum by Miles^{2, 8} and the anatomic description of the lymphatic system of the rectum and anus by Delamere, Poirier, and Cuneo,³ three collecting systems are present, the superior, lateral, and inferior routes of lymphatic drainage corresponding to the superior, middle, and inferior hemorrhoidal veins and classified by Miles as the extramural lymphatics into which the intramural and intermediary systems drain. The intramural lymphatics consist of two freely communicating networks located within the wall: one, the submucosal, and the other, the intermuscular network. These intercommunicate by the radial lymph channels lying between the circular muscle fibers. The submucosal network is to a lesser extent continuous, above, with the pelvic colon, and below, with the subcutaneous lymph channels of the

perianal skin. The tendency of carcinoma to spread through the submucosal network (Fig. 3A) does not appear to be as common as to spread by the radial channels into the deeper intermuscular network (Fig. 3B). The intermuscular network lying between the circular and longitudinal muscle coats communicates with similar channels of the pelvic colon above, and below with those of the external sphincter



Fig. 3A.—Photomicrograph of submucosal lymph channels showing neoplastic emboli.

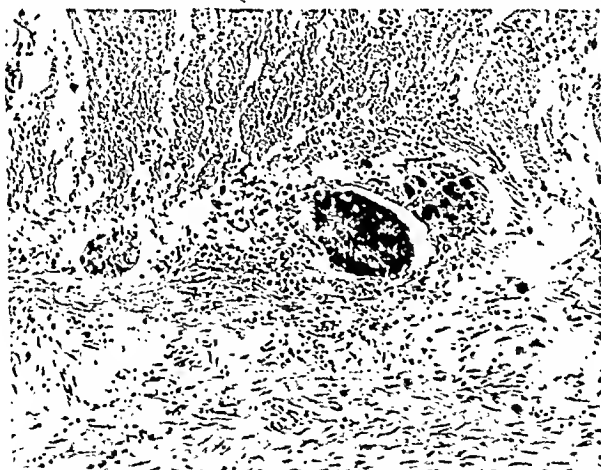


Fig. 3B.—Photomicrograph demonstrating neoplastic emboli in the intermuscular lymphatic network.

muscles. The main avenue of dissemination, however, is through the external muscle coat to the intermediary system, which consists of two parts, a subserous network in that portion of the rectum invested with a peritoneal covering, and a lymph sinus, situated between the external muscular coat and the perirectal fat in that part of the rectum beneath the peritoneal reflection.

The third lymphatic system, and the one which is most important surgically, is the extramural. The efferent channels from the lymph sinuses and subserous lymph channels form an extensive plexus which drains into the anorectal glands of Gerota which are scattered over the lateral and posterior aspects of the rectum and lie in the hollow of the sacrum. The efferents of these drain into the lymph channels accompanying the superior hemorrhoidal vein (the superior zone of spread) (Fig. 3C), into the middle hemorrhoidal vein (the lateral zone of spread), or if the lesion is low enough, into the lymph channels accompanying the inferior hemorrhoidal vein (the inferior zone of spread). Cancer cells thus may metastasize in any one of the three zones of spread, upward, laterally, or downward. There are many cases showing evidence of metastases in more than one zone of spread, this being especially true of carcinoma of the anal canal. Spread by the inferior zone may occur along the subcutaneous perianal lymph channels in the perineum to the inguinal lymph nodes or through the ischiorectal fossa, Alcock's canal, and into the internal iliac lymph nodes. In untreated cases and in those which have recurrences, it is not uncommon to find carcinomatous nodules in the perineum, rectovaginal septum, and ischiorectal fossa. Consequently, operative removal should include wide excision of the perianal skin, ischiorectal adipose tissue, and levator ani muscles.



Fig. 3C.—Photomicrograph demonstrating neoplastic emboli in the extramural collecting system accompanying a large blood vessel.

The lateral efferent lymphatics drain into a number of channels accompanying the middle hemorrhoidal vessels and lie between the pelvic peritoneum, endopelvic fascia, and levator ani muscles. These also eventually drain to the lymph nodes along the internal iliac veins. This route of spread was beautifully demonstrated by an autopsy case in which retroperitoneal dissection of the entire contents of the lower abdominal, pelvic, and inguinal regions was made (Fig. 4).

The upward zone of spread is along the lymph channels and nodes in the retrorectal and retrocolic position accompanying the superior hemorrhoidal vessels along the base of the sigmoid mesocolon and continuing with the inferior mesenteric vessels.

Lymphatic vessels differ from the blood vessels in that, instead of one or two channels draining the same area, the lymph is returned by several channels which tend to form a plexus about the blood vessels. There may also be a number of efferent vessels to any one node, thus explaining the observation that contiguous lymph nodes are not necessarily involved and that the nodes at various levels may be implicated. Lymph nodes act as barriers to filter out neoplastic emboli. A neoplastic embolus enters a lymph node by its peri- and subcapsular lymph channels (Fig. 2). If the metastasis remains viable, it sets up a new neoplastic focus, tending to block the lymph channel, which then

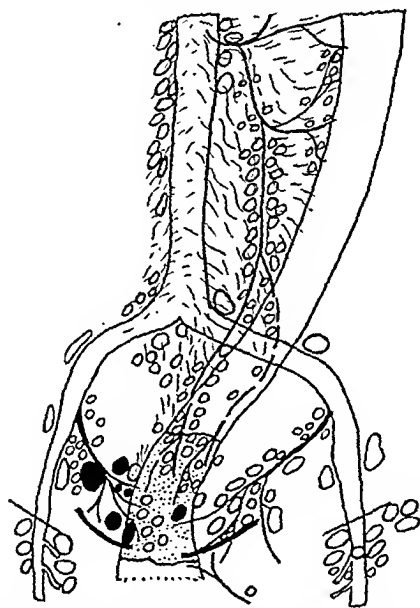


Fig. 4.—Line drawing of an autopsy specimen illustrating the lateral zone of lymphatic spread from an adenocarcinoma, Grade II, of the anal canal; 170 lymph nodes isolated, 7 of which, lying along the right middle hemorrhoidal artery, are replaced by metastatic carcinoma.

becomes dilated and distended with lymphocytes. Lymph flow becomes static and other neoplastic foci may be established along the lymph channels. It is therefore common to find multiple small neoplastic nodules in the perirectal adipose tissue. The direction of lymphatic metastases depends on the direction of the lymph flow, and, if it becomes obstructed by neoplastic emboli, the lymph will then find unobstructed channels. Not until there have been extensive metastases along the superior zone of spread do all or a majority of the lymph channels become sufficiently obstructed to cause a retrograde flow of lymph. In our cases, even in those with extensive metastases, we had no evidence

of retrograde metastases to nodes situated a significant distance below the primary site, in contradistinction to the four cases reported by Gilehrst and David. In seventy-four cases studied by Westhus⁴ there was evidence in only one instance of retrograde metastasis. This undoubtedly does occur, but it must be exceedingly rare.

From a surgical viewpoint, the extramural lymphatics are of more importance than the intramural. An understanding of the intramural lymph channels, however, is important in order to realize how superficial malignancies involving only the submucosa and muscular layers may metastasize.

AGE AND LYMPH NODE METASTASIS

The average age was 53.3 years in those with metastases and 53.5 years in those without. In analyzing the cases by decades (Table I) there was no significant variation found. Grouping the cases into those below and those above 50 years of age, it was found that 70 per cent in the younger age group had metastases in comparison to 60.6 per cent in the older. The only carcinoma of histologic Grade IV was in the 20- to 30-year age group.

TABLE I
CORRELATION OF DECADE OF LIFE AND METASTASES

| DECADE | NUMBER OF CASES | WITHOUT METASTASES | | WITH METASTASES | |
|--------|-----------------|--------------------|------------|-----------------|------------|
| | | NUMBER OF CASES | PERCENTAGE | NUMBER OF CASES | PERCENTAGE |
| 20-30 | 2 | 0 | 0 | 2 | 100 |
| 30-40 | 6 | 3 | 50 | 3 | 50 |
| 40-50 | 12 | 3 | 25 | 9 | 75 |
| Totals | 20 | | | 14 | 70 |
| 50-60 | 14 | 7 | 50 | 7 | 50 |
| 60-70 | 17 | 5 | 29.4 | 12 | 70.6 |
| 70-80 | 2 | 1 | 50 | 1 | 50 |
| Totals | 33 | | | 20 | 60.6 |

In a correlation of age and degree of malignancy in carcinoma of the colon by Rankin and Broders,⁵ it was reported that carcinoma in younger age groups tended to be of a higher grade of malignancy than in the group as a whole, and because of this there was a greater tendency to metastasize. This is undoubtedly true, but there are other factors present in younger individuals which also influence the tendency of neoplasms to metastasize. Fascial planes and connective tissue are known to act as a barrier to the advancing malignancy. Lymph and blood vessels in elderly people are thickened by deposition of connective tissue in their walls, thus presenting more of a barrier to infiltration.

DURATION OF SYMPTOMS AND METASTASES

No relation existed between duration of symptoms and the occurrence of metastases. There was an average duration of symptoms

of 8.42 months in the cases in which metastases had occurred, and 9.44 months in the group in which metastases had not occurred. This illustrates the point that the case with the shortest history is not always the most favorable for treatment. There were three patients in the series with symptoms of rectal carcinoma for one month or less who yet had lymph node metastases. There were other patients without any symptoms who, upon routine physical examination, were found to have rectal carcinomas that were later discovered to have metastasized. There were four patients with symptoms of 1 year's duration, one of 1.5 years, and another of 2 years, whose specimens showed no evidence of regional lymph node involvement. One of these patients was given up as hopeless 1.5 years prior to admission to this hospital. Duration of symptoms alone should not influence the treatment advised.

GROSS TYPES OF RECTAL CARCINOMAS

Carcinoma of the rectum was classified by its gross characteristics into three groups. The first group included the large, fungating, polypoid neoplasms, the majority of which arose in polypi. With these were included those carcinomas which were originally polypoid, but whose centers had undergone necrosis and ulceration so that they had become ulcerated with a polypoid, rolled, everted border. It was felt that central ulceration had occurred, either because of outgrowing their blood supply or because of ischemia as the result of neoplastic occlusion of the blood vessels. Most of them had marked infection and inflammatory changes within their substance. The second group included the sessile or plaque-like neoplasms which infiltrate the bowel wall. In the third group the lesion was excavated to form a deep ulcer. A correlation of these gross types with lymphogenous metastases (Table II) confirmed the opinion of others⁶ that lesions tending to grow out into the lumen are less malignant than those infiltrating deeply into the wall.

TABLE II
CORRELATION OF GROSS TYPES AND LYMPH NODE METASTASES

| GROSS TYPES | NUMBER OF CASES | WITH METASTASES | WITHOUT METASTASES | PERCENTAGE OF METASTASES |
|-------------|-----------------|-----------------|--------------------|--------------------------|
| Excavating | 3 | 1 | 2 | 33 |
| Polypoid | 28 | 15 | 13 | 53.5 |
| Sessile | 21 | 17 | 4 | 80.9 |

Of the 3 excavating lesions, only 1 (33 per cent) had metastasized; of the 28 polypoid neoplasms, 15 (53.5 per cent) had metastasized; whereas, in the 21 sessile neoplasms, 17 (80.9 per cent) had metastasized, showing that this latter type of malignancy has a very much higher probability of metastasizing. An excellent example of the lower grade of malignancy of polypoid carcinomas is illustrated by one of our patients who had a huge fungating polypoid neoplasm

measuring 11.5 by 7.5 cm. in diameter, beginning at the mucocutaneous junction, completely encircling the lumen, and extending upward as far as the finger could reach. This appeared to be fixed to the prostate anteriorly and was thought to be inoperable. This patient was a poor surgical risk because of his age, obesity, and hypertension. Because of intestinal obstruction, a sigmoid colostomy was done. No evidence of hepatic or peritoneal metastases was found. Two weeks later he died of pulmonary embolism. The entire lower abdominal and pelvic contents were dissected retroperitoneally and cleared, and 257 lymph nodes were isolated from the three zones of spread, including those along the abdominal aorta, the internal and external iliac vessels, and inguinal regions. No metastases were found. This case illustrates three points: (1) that huge lesions in themselves do not contraindicate resection, or at least laparotomy to determine operability; (2) that polypoid neoplasms tend less to metastasize; and (3) that fixation of the growth to the prostate may be inflammatory rather than neoplastic. Nevertheless, over 50 per cent of the polypoid neoplasms had metastasized and there is no means of determining which of these lesions have or have not done so. The one observation that is valuable is that sessile, plaque-like neoplasms have a high percentage of metastases.

METASTASIS AND LEVEL OF LESION

The lesions were classified according to their distance above the mucocutaneous junction in order to correlate location with the occurrence of lymphatic metastases. The neoplasms were divided into four groups: (1) those arising within the anal canal up to and including 2.5 cm. above the mucocutaneous junction; (2) those within the ampulla of the rectum, which we arbitrarily placed between 2.5 to 9.5 cm. above the mucocutaneous junction; (3) those of the rectosigmoid, which, according to anatomists, vary from 10 to 15 cm. above the mucocutaneous junction; and (4) those carcinomas arising from the sigmoid colon above 15 cm. from the junction.

There were 18 adenocarcinomas and 1 spindle-cell sarcoma arising within the anal canal and low rectum. Of these, 8 had not metastasized, and 11, including the spindle-cell sarcoma (57.9 per cent), had. Of those 11 neoplasms which had metastasized, 6 had spread along the superior zone in lymphatics accompanying the superior hemorrhoidal vessels as well as along the lateral zone of spread accompanying the middle hemorrhoidal vessels (Fig. 5A). In the remaining 5 cases, metastases were found along the superior zone of spread only (Fig. 5B). Of the 11 cases that had metastasized, 3 had three or less lymph nodes involved; in 2 of these the involved nodes were located at the primary site. In an additional 3 cases in which four or more nodes were involved, the positive nodes were located close enough to the primary site to be included in a perineal resection as far as the superior

zone of spread alone is concerned. Thus, 13 of the 19 cases (68.4 per cent) of the lesions in the anal canal and low rectum were amenable to perineal resection in respect to the superior zone of spread.

It is interesting to note, however, that seven specimens, or 36.8 per cent of the total of 19 cases in this region, showed evidence of lymph node involvement up to the margin of excision of the levator ani muscles along the lateral zone of spread (Fig. 5A). This emphasizes the importance of wide excision of the tissues of the lateral zone of spread as well as the superior zone of spread in operating on low-lying rectal carcinomas and those of the anal canal.

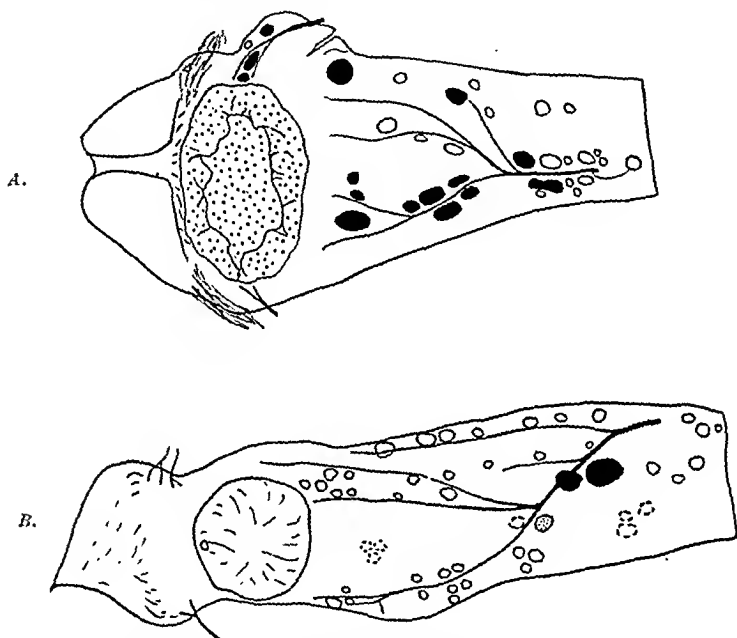


FIG. 5.—A, Line drawing illustrating a far-advanced adenocarcinoma mucosum, Grade III, of the anal canal; 33 lymph nodes isolated, 15 of which, lying along the superior and lateral zones of spread, are largely replaced by carcinoma. B, Line drawing illustrating an adenocarcinoma of the anal canal; 50 lymph nodes isolated, 3 of which, lying at a considerable distance from the primary site, are largely replaced by carcinoma.

Six cases (31.5 per cent) of the total 19 showed lymph node involvement along the superior zone of spread which would have been beyond the reach of a perineal resection (Fig. 5B). Of these 6 cases showing metastases in lymph nodes at a considerable distance above the primary neoplasm, 2 showed nodes to be involved up to the site of ligation of the superior hemorrhoidal vessels, so that in all probability there may be residual carcinoma, even following a combined abdominal-perineal resection. The specimen shown in Fig. 5B had no metastases to the immediate regional lymph nodes, but did have metastases in lymph nodes at a considerable distance above the lesion.

In summarizing this group, theoretically 68.4 per cent of the patients could have been completely cured by perineal resection if the lymphatic

spread of carcinoma were the only factor involved, but 31.5 per cent of the anal and low rectal lesions would not have been cured by perineal resection. However, 10.5 per cent (2 cases) probably were not cured because of high involvement of the lymphatics, by combined abdominal-perineal resection with high ligation of the superior hemorrhoidal vessels. Thus, 21.1 per cent more cases would be cured by the more extensive operation.

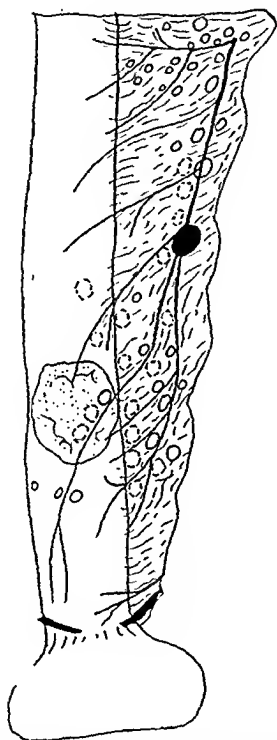


Fig. 6.—Line drawing illustrating an advanced papilliferous adenocarcinoma, Grade II, of the rectal ampulla: 50 lymph nodes isolated, 1 of which, lying 5 cm. from the primary site, is completely replaced by carcinoma.

There were 21 cases of carcinoma of the rectal ampulla, 8 without metastases and 13, or 61.9 per cent, with metastases. In every instance the lymphatic spread of carcinoma of the rectal ampulla was along the superior zone. Some of the lesions which were partly within the rectal ampulla but whose inferior edges were less than 2.5 cm. above the mucocutaneous junction have already been considered with the low-lying lesions. In no lesion of which the inferior border was 3 cm. or more above the mucocutaneous junction did we find metastases along the lateral zone of spread. Of the 13 cases with metastases in the lymph nodes, in 2 the involved nodes were confined to the region of the primary site; 2 more had positive nodes at least 5 cm. above the primary site (Fig. 6), and in 2 the metastases were 10 cm. or more away from the neoplasm without involvement of the intervening nodes.

In another case (Fig. 7A) nodes were invaded near the primary site and none involved until a point 10 cm. higher at the site of ligation of superior hemorrhoidal vessels. In other cases, such as Fig. 7B, nodes were involved in a continuous chain from the primary neoplasm to within a short distance of the site of ligation. Only one of the carcinomas in the rectal ampulla with metastases would have been suitable for a perineal resection. As seen in the diagrams of cleared specimens, the majority of cases present differences in direction of lymphatic spread between the lesions of the ampulla and of the rectosigmoid and sigmoid colon. The lymph node metastases of carcinoma of the ampulla lie along the lymph channels which accompany the vessels so that they

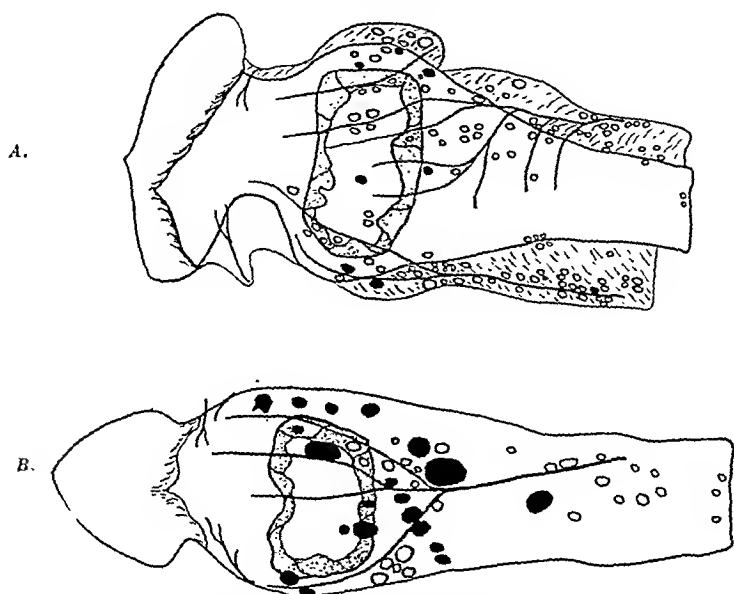


Fig. 7.—A, Line drawing illustrating an adenocarcinoma, Grade II, of the rectal ampulla; 123 lymph nodes isolated, 7 of which, near the primary site, and 1 at the level of ligation of the superior hemorrhoidal artery, show metastatic carcinoma. B, Line drawing illustrating an adenocarcinoma mucosum, Grade II, of the rectal ampulla; 46 lymph nodes isolated, 19 of which, about the primary site and in a continuous chain nearly to the level of ligation of the superior hemorrhoidal artery, are largely replaced by metastatic carcinoma.

run upward almost parallel with the course of the rectum. Consequently, the lesions of the ampulla must be more widely excised than those of the rectosigmoid colon where the lymph channels tend to run perpendicular to the bowel. Lesions of the rectosigmoid and sigmoid should have a greater depth of mesentery excised. It will be noted also that there were fewer involved lymph nodes for each case in carcinoma of the ampulla than in lesions of the anal canal and low rectum.

There were six cases of carcinoma of the rectosigmoid. Five of these (83.3 per cent) had metastasized, only one node being involved in two instances; two in the third (Fig. 8A), the involved nodes being adjacent to the primary site; and in the other two cases, lymph nodes were in-

volved 5 and 10 cm. above the primary site. There was evidence of retrograde metastases in one of these cases in that one positive node was located 1.5 cm. below the lesion. Considering only regional lymph node involvement, four cases (66.6 per cent) would have been just as suitable for wide resection with preservation of the low rectum as for combined abdominal-perineal resection.

There were 6 cases of carcinoma above the rectosigmoid junction in the group. All of the involved nodes in the 4 cases which had metastasized to lymph nodes were located near the primary site (Fig. 8*B*), making them also suitable for reconstructive operation as far as lymphogenous metastasis is concerned.

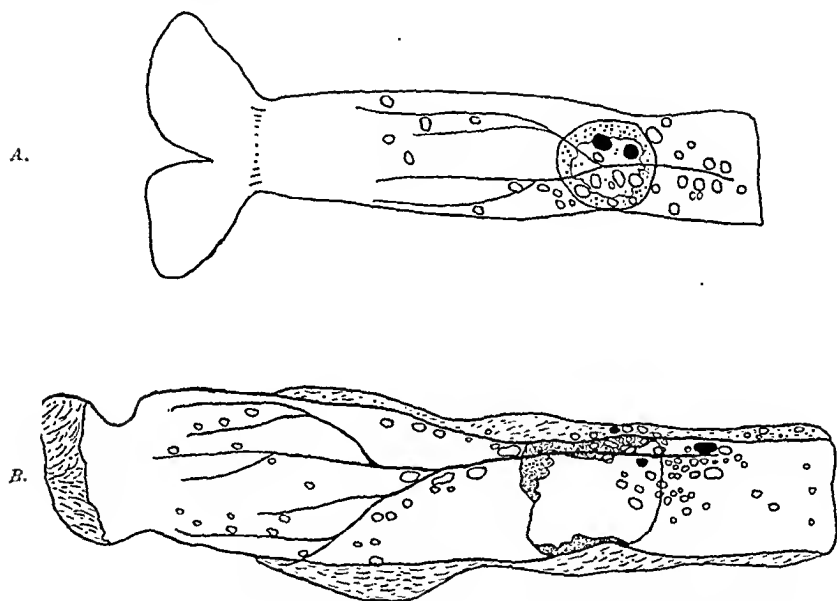


Fig. 8.—*A*, Line drawing illustrating an advanced ulcerative papilliferous adenocarcinoma, Grade III, of the rectosigmoid, infiltrating through the wall and into adjacent adipose tissue; 35 lymph nodes isolated, 2 of which show metastatic carcinoma at the primary site. *B*, Line drawing illustrating a widespread infiltration of adenocarcinoma, Grade II, of the low sigmoid colon; 88 lymph nodes isolated, 3 of which, lying near the primary site, show metastatic carcinoma.

SITE OF ORIGIN UPON CIRCUMFERENCE OF BOWEL WALL AND METASTASES

There have been varying opinions expressed as to the site of origin upon the circumference of the bowel wall and the likelihood of metastases. Any correlation of this sort is difficult because rarely, unless the lesion is very small, is it confined to one wall alone. Usually the lesion involves several walls and often is annular. If the lesion was of such a size as to involve two walls, i.e., anterior and lateral walls, we classified it as such; in an extensive lesion it was placed with that part corresponding to its center. In the correlation, the anterolateral and posterolateral lesions were classified in either the anterior or posterior

group and to the lateral wall group. Eight cases of annular neoplasm in which the site of origin was impossible to determine were excluded. The anterolateral and posterolateral lesions were considered as being either upon the posterior or anterior wall. It appeared that the anterior wall neoplasms were slightly more likely to metastasize. This observation is even more striking when these same neoplasms, i.e., those on the antero- and posterolateral walls, were in the lateral group. In this particular instance 85.4 per cent of those on the anterior or antimesenteric wall had metastasized to the regional lymph nodes.

SIZE OF NEOPLASMS AND METASTASES

There was found no relation between the size of the lesion and the presence of metastases. The average size of all lesions was 5.8 by 4.5 cm. There were 8 cases without metastases and 18 cases with metastases in lesions of less than average size. In the group of neoplasms larger than average size, there were also 8 cases without metastases and 18 cases with metastases. The 10 smallest carcinomas and the 10 largest carcinomas were compared, and in each group there were 6 cases with and 4 cases without metastases. The two largest carcinomas, whose areas were 85 and 79.25 sq. cm., respectively, had no metastases. The next largest size was 49 sq. cm. and this also had not metastasized to the lymph nodes. The largest size to have metastasized was 42.5 sq. cm. and this case had only two positive lymph nodes in 51.

EXTENT OF BOWEL CIRCUMFERENCE INVOLVED AND METASTASES

Whereas there was no relationship between the size of the carcinoma and the lymph node metastases, it seems true that there is a slight increase in likelihood of metastases as more of the bowel circumference is involved by the malignancy. The neoplasms were divided into four groups, depending upon the percentage of the bowel circumference involved (Table III). There was a slightly increasing tendency for the neoplasm to metastasize as it spread around the bowel wall. It appears that the extent of the circumference involved is of more importance in determining the likelihood of metastases than the longitudinal extent of the lesion.

TABLE III
CORRELATION OF CIRCUMFERENCE OF WALL INVOLVED AND METASTASES

| PERCENTAGE OF CIRCUMFERENCE INVOLVED | NUMBER OF CASES | WITHOUT METASTASES | WITH METASTASES | PERCENTAGE WITH METASTASES |
|--------------------------------------|-----------------|--------------------|-----------------|----------------------------|
| 0-25 | 4 | 2 | 2 | 50 |
| 25-50 | 10 | 4 | 6 | 60 |
| 50-75 | 22 | 8 | 14 | 63.6 |
| 75-100 | 17 | 5 | 12 | 70.6 |

DEGREE OF CELLULAR DIFFERENTIATION (GRADING) AND METASTASES

Most of the carcinomas of the rectum were graded II and III as to cellular differentiation. There was only one Grade IV neoplasm, a carcinoma developing in a bowel the site of a chronic ulcerative colitis in a girl 24 years old. The entire rectum and rectosigmoid, except for the anal canal, were found to be infiltrated diffusely by a poorly differentiated adenocarcinoma that had spread through the entire wall and showed carcinomatous cell nests in both the lymph and blood channels. Seventy of 100 lymph nodes isolated were largely replaced by metastatic carcinoma. The patient died three months later, at which time she showed further carcinomatous proliferation in the transverse and ascending colon. The only carcinoma graded I, not listed in the table, was found in a polyp which accompanied a large carcinoma. Table IV substantiates the dictum that the more anaplastic the lesion, the more likely the presence of lymph node metastases. However, the surgeon should not base his surgical procedure solely upon histologic grading of biopsy specimens. It is a common experience to find that, after having examined the specimen as a whole, the opinion based on the biopsy must be altered. It is impossible to grade the carcinoma as a whole by examining only one small portion of it. Degree of malignancy, size of lesion, and operability are not synonymous terms and should not be used interchangeably. Often the more malignant neoplasms are the smaller and in turn are the more favorable operative cases from the technical aspect. These lesions are highly malignant and give rise to early metastases. An illustration that grading of the biopsy specimen does not represent the tumor as a whole is shown in a case in which the biopsy specimen was taken at the infiltrating border and graded IV. Because the lesion was assumed to be very highly malignant, fixed to the prostate, and because the patient was a poor operative risk, a palliative colostomy only was done. The patient died and the autopsy specimen showed a moderately well-differentiated adenocarcinoma, graded III, with no evidence of metastases.

TABLE IV
CORRELATION OF GRADE OF MALIGNANCY AND METASTASIS

| GRADE | NUMBER OF CASES | WITHOUT METASTASES | WITH METASTASES | PERCENTAGE WITH METASTASES |
|-------|-----------------|--------------------|-----------------|----------------------------|
| I | 0 | 0 | 0 | 0 |
| II | 33 | 14 | 19 | 57.5 |
| III | 18 | 5 | 13 | 72.2 |
| IV | 1 | 0 | 1 | 100 |

Gabriel, Dukes and Bussey⁷ classified carcinomas of the rectum into Groups A, B, and C. Group A included cases where the carcinoma infiltrated well into the wall but not into the perirectal tissues; Group B, those in which the carcinoma extended into the perirectal tissue;

and Group C, those having positive lymph node metastases. They found that 91 per cent of Group A cases and 64 per cent of Group B cases were alive for five years or more following operative removal; whereas, in Group C, those having glandular metastases, only 18 per cent survived five years. This classification in its last analysis really compares the prognosis of cases with metastases and those without. It was difficult for us to fit our cases into this classification. We had 30 cases in which the malignancy was confined to the rectal wall. Of these, 13 (43.3 per cent) had metastasized to the regional lymph nodes; whereas we had 22 cases which had infiltrated into the perirectal tissues, of which 20 (90.9 per cent) had given rise to metastases. This comparison, we believe, is of more value.

The histologic types of carcinoma and the percentages of metastases are shown in Table V. The most common type was adenocarcinoma; the next most common was papilliferous adenocarcinoma, several of which were papilliferous cystadenocarcinoma. The likelihood of metastases of these types is approximately the same, in that 61.2 per cent of the first and 61.5 per cent of the second gave rise to lymph node involvement. There were four cases of adenocarcinoma mucosum, all of which had metastasized and in which the extent of metastases was also great. Adenocarcinoma mucosum is generally considered to be the most malignant type, this observation being borne out by this small series. There were three cornifying squamous-cell carcinomas of the anal canal and mucocutaneous junction; another, which was partly adenocarcinoma and partly cornifying squamous-cell carcinoma; and one spindle-cell sarcoma.

TABLE V
CORRELATION OF MICROSCOPICAL TYPES AND METASTASES

| MICROSCOPICAL TYPES | NUMBER OF CASES | WITHOUT METASTASES | WITH METASTASES | PERCENTAGE WITH METASTASES |
|--|--------------------|-----------------------|--------------------|----------------------------------|
| Adenocarcinoma | 31 | 12 | 19 | 61.2 |
| Papilliferous adenocarcinoma | 13 | 5 | 8 | 61.5 |
| Adenocarcinoma mucosum | 4 | | 4 | 100 |
| Cornifying squamous- cell carcinoma | 3 | 1 | 2 | 66.6 |
| Adenocarcinoma and squamous cell | 1 | 1 | 0 | 0 |
| Spindle-cell sarcoma | 1 | | 1 | 100 |

Finally, the point that has been brought out by numerous other observers, but which can be re-emphasized, is the close relationship between carcinoma of the rectum and rectal polyps. In the 53 cases studied, there was microscopic evidence of the malignancy arising upon pre-existing polyps in 28.3 per cent of the cases (15 of 53 cases). Twenty-two other cases (41.5 per cent) also had associated polyps,

varying from one to six polyps per specimen. Examination of one such polyp 3 mm. in diameter showed early carcinomatous proliferation. Two additional cases were associated with polyposis of the colon. There is microscopic evidence to show the progression from simple hyperplasia of the rectal mucosa through the formation of small adenomas or polyps, to the development of frank carcinoma. Both the sessile and larger pedunculated polyps may show marked atypical hyperplastic proliferation of the mucous membrane but no infiltrative growth. It is not necessary for the polyp to be either large or pedunculated, for very small, innocuous-appearing, sessile polyps may be the basis of malignant change.

SUMMARY

A study was made of metastasis from carcinoma of the rectum and rectosigmoid to the regional lymph nodes in 53 specimens, and an average of 68 nodes per operative specimen were isolated and examined microscopically. They were charted and the results correlated with various physical attributes of the associated primary lesion.

Lymph nodes were found at the site of metastases in 64 per cent of the carcinomas of the rectum and 15 per cent showed invasion of the blood vessels.

Age of the patient had no important influence on the presence of metastases in lymph nodes as 70 per cent of the patients below 50 years of age had them, while of those over 50 years, metastases were present in 60 per cent.

A comparison of the incidence of metastases in carcinoma of the rectum classified according to their gross characteristics as sessile, excavating, and polypoid showed 80.9 per cent of the sessile type to have produced metastases; in 33 per cent of the excavating and only 53.5 per cent of the polypoid neoplasms had this occurred.

The only lesions having involvement of lymph nodes along the lateral zone of spread were those arising between the synchronous junction and a point 3 cm. above it.

In no instance was found retrograde metastasis to a significant level below the primary lesion. No relation was found to exist between the size of the tumor and the presence of metastases in lymph nodes.

No correlation was found between the size of the lymph nodes and the presence in them of metastases.

If the lesion had infiltrated through the wall of the rectum, lymph nodes were involved in 90.9 per cent in comparison to those lesions that were still confined to the wall in which 43.3 per cent had metastases in lymph nodes.

As far as could be determined, 28 per cent of the neoplastic lesions developed in polyps and another 41.5 per cent of the specimens had benign polyps present.

Neoplasms arising on the anterior wall had the larger percentage of lymph node metastases.

Involvement of lymph nodes and operability are not dependent on duration of symptoms.

Surgical procedure should not be based solely on the histologic grading of biopsy specimens.

The prognosis in any case can be made more accurately by an examination of all of the lymph nodes.

In spread of carcinoma along any zone of diffusion the nodes are not necessarily involved in continuity but may be involved at some distance with normal nodes intervening between the primary site and the metastases.

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INTERNAL SUPRAVESICAL HERNIAS

WESLEY N. WARVI, M.D., AND THOMAS G. ORR, M.D., KANSAS CITY, KAN.
(From the University of Kansas Hospitals)

THIS REVIEW and diseussion of internal supravescical hernias, including a report of an additional case, show that this condition is much less rare than previously believed, that a preoperative diagnosis of the condition is difficult but possible, and that the prognosis in each case depends upon early proper treatment.

Authors have disagreed on the anatomic terminology in describing the site of the lesion as well as on the nomenclature of the hernias originating in the supravescical fossa. Our conclusions have been reached after a review of all available literature on this subject.

ANATOMY

The supravescical fossa is a triangular area bounded laterally and above by the lateral umbilical folds which cover the obliterated umbilical arteries, and below by the peritoneal reflection that passes from the anterior abdominal wall to the fundus of the bladder. The median umbilical fold, formed by the remnant of the urachus, divides the supravescical fossa into right and left halves. Pick¹ and others believe this area should extend posteriorly along each side of the bladder to the point where the lateral umbilical folds blend into the peritoneum of the true pelvis and thus include the retrovesical fossa in the male and the vesicouterine fossa in the female. Very few authors agree with this extension of the limits of the fossa because it would make the boundaries too obscure and too inclusive.

Supravescical fossa is the name most widely accepted since its introduction by Waldeyer² in 1874. Other names used to designate this region are: vesicoinguinal fossa by Velpeau,³ fossa vesicomedialis by Brentano,⁴ fossa interligamentosa by Draudt,⁵ internal inguinal fossa by Kadlieky,⁶ fovea medialis by Cestmir,⁷ paravesical fossa by Pick, and the fovea inguinalis intima by Joessel.⁸

NOMENCLATURE OF HERNIAS

The chaotic multiplicity of terms used in the past in referring to internal supravescical hernias can be illustrated by enumerating twenty-two of them in the order in which they have appeared in publications. Ring⁹ first described a case as an internal inguinal hernia in which he referred to Cooper's¹⁰ work published in 1804 (Fig. 1). Other names used were: hernia inguinalis media antevesicalis by Parise,¹¹ properitoneal diverticula with intestinal incarceration by Hartung,¹² hernia retroperitonealis parietalis hypogastrica by Linhart,¹³ anterior retro-

peritoneal hernia by Klebs,¹⁴ properitoneal hernia by Kronlein,¹⁵ vesicopubic hernia by Havage,¹⁶ hernia diverticula parietoinguinalis, a later name used by Kronlein to differentiate it from herniae *en bissac*, oblique internal or suprapubic inguinal hernia by Lupo,¹⁷ prevesical hernia by Kaufmann,¹⁸ anterior retroperitoneal hernia by Wilms,¹⁹ supravescical hernia by Waldeyer, prevesical epiplocele in a case of Makins²⁰ which contained omentum, properitoneal supravescical hernia by Maydl,²¹ hernia inguinalis obliqua interna by Joessel, prevesical properitoneal hernia by Kadlicky, retroperitoneal bladder hernia of the supravescical fossa by Steimker,²² oblique internal hernia by Luttel-

PLATE 3.

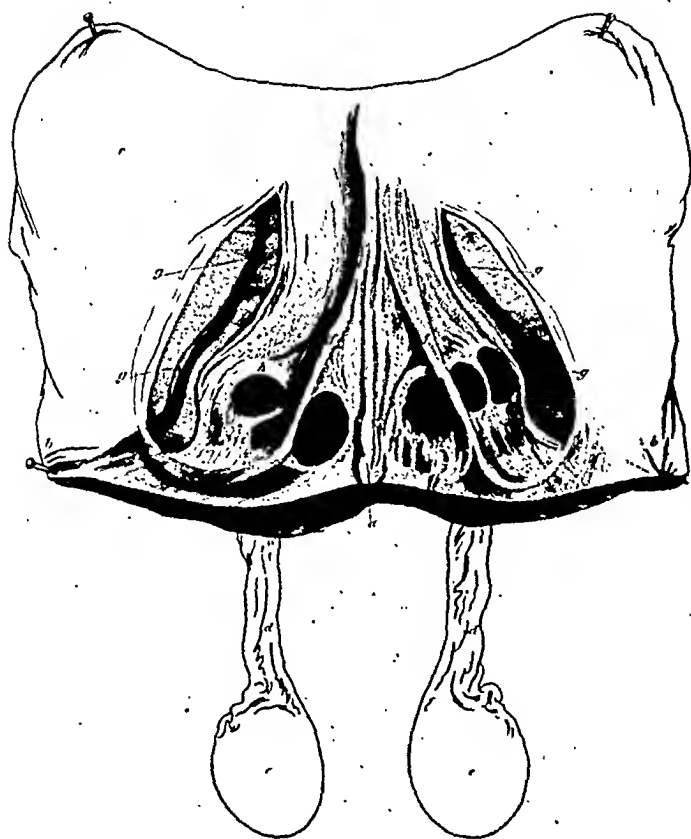


Fig. 1.—This plate appeared in Sir Astley Cooper's book *The Anatomy and Surgical Treatment of Internal and Congenital Hernia*, published in 1804. It shows six hernial openings, two of which are in the supravescical fossa. This is probably the first reference to supravescical hernia.

mann,²³ and paravesical hernia by Pick. In addition there were four terms noted by Blum²⁴ which had been used by various authors when an internal supravescical hernia protruded into the bladder apex which were: intravesical hernia of the supravescical fossa, invaginatio vesicae, inversio vesicae urinariae incompleta, and cystanestrophe. This varied nomenclature may explain why there have been but six authentic cases of supravescical hernias collected in the past.

The logical name is one indicating the place of origin of the hernia with added terms to indicate the direction taken by the herniation, the place of lodgement of the hernial sac, and possibly the character of the hernial contents. With this in mind we believe the term supravescical is the most suitable for hernias originating in the supravescical fossa. These hernias can be further classified into external, internal, and perhaps interstitial types. The external types appear in the hypogastrium or in the inguinal, femoral, and obturator regions. The internal supravescical hernias can be prevesical, intravesical, paravesical, or lateral dependent upon lodgement in the space at Retzius, in the bladder, beside the bladder, or in the more lateral pelvis respectively. Definite examples of interstitial types have not been recorded.

Other classifications and terms are not acceptable because they are misleading and indefinite. The classification of Walker²⁵ included only three possible types which he recognized as arising from the supravescical fossa. They were prevesical for the internal type, hypogastric for those appearing directly anteriorly and externally, and a third group described as passing through the femoral canal and often mistaken for true femoral hernias. The term prevesical, when used alone to designate internal supravescical hernias in the space of Retzius, is misleading because hernias originating in the inguinal regions may extend medially to the prevesical space as exemplified by the case reports of Makin, Parise, and Oberst.²⁶ Also the use of the term paravesical alone, as applied to supravescical hernias by Pick, has the same objection, since hernias arising in the inguinal region may extend medially as they descend into the pelvis and may lodge in the paravesical space adjacent to the bladder. Kaufmann reported a case of this kind.

ETIOLOGY AND PATHOGENESIS

According to Finsterer,²⁷ the primary etiologic factor underlying the formation of supravescical hernias is an abnormality in the regression of fetal structures causing a congenital predisposition to hernias because of the depth of the supravescical fossa. Rokitsansky²⁸ also emphasizes the part played by raised fibrous bands, due to delayed regression of the umbilical arteries and urachus, so that they stand out from the anterior abdominal wall raising mesentery-like peritoneal folds and forming deep fossae between them. These fossae further develop into deep diverticula due to the loss of prevesical fat, fibrotic retraction

following subperitoneal inflammations, peristaltic action of lodged loops of intestines, the dilating wedge effect of omentum or lipomas of the bladder, and finally because of sex differences in pelvic anatomy and physiology so that males are more often affected. The bladder filling in males causes an anterosuperior enlargement that traps intestines in supravescical diverticula when present, while in the female the distention of the bladder occurs laterally and forces supravescical diverticular contents upward and outward.

General etiologic factors in common with the formation of hernias elsewhere are: congenital weakness of connective tissue with coneomitant hernias at other sites, fatty infiltration of connective tissue during obesity so that weight loss results in pathologic enlargement of natural openings, and persistent organic or repeated functional increases in intra-abdominal pressure which cause peritoneal outpouchings at the weakest points.

After a supravescical diverticulum has developed it can herniate in any one of five possible directions, depending upon the path of least resistance (Fig. 2). Those of the superomedial part, making up the greatest number of cases, protrude externally in the hypogastrium. Those of the superolateral part evaginate toward the inguinal, femoral, or obturator regions. The inferomedial protrusions become lodged in the prevesical space of Retzius or when the bladder apex is weakened by defective closure of the urachus, as in cases reported by Forster²⁹ and Markel,³⁰ they herniate directly into the bladder. The fifth possibility is the extension of the herniation caudally as far as the prostatic bed lateral to the bladder in the male, or to the base of the broad ligament in the female. The last three groups arising from the inferior portion of the fossa never appear externally because they are below the rigid wall of the anterior pelvis.

Spontaneous reduction of internal supravescical hernias can occur, as evidenced by finding empty hernial sacs after symptoms of visceral lodgement. Korte³¹ reports 1 case and Robinson³² 2 cases in living subjects; while Reich,³³ Pick, Tandler and Halban,³⁴ and Mareoni³⁵ report a total of 8 cases of empty hernial pockets found post mortem. Cooper's case was probably also of this type.

Hernias originating in the supravescical fossa are more numerous than the reviews of the past indicate. A multiplicity of names applied to these hernias reported in various languages has apparently been a source of difficulty in attempted reviews. That these hernias have been overlooked is attested by the absence of a definition of the term in modern medical dictionaries as well as by the absence of any reference to them in such publications as Watson,³⁶ Carrera,³⁷ and numerous earlier works.

Supravescical hernias appearing externally are most numerous. Reich³⁸ reviewed 26 cases in 1909 and several publications have appeared on

TABLE I

| NO. | AUTHOR | DATE | AGE | SEX | LOCATION | CONTENTS OF SAC | DURATION OF SYMPTOMS | TYPE | RESULTS |
|-----|----------------------|------|-----|-----|--|--|-----------------------------|--|-----------------------------------|
| 1 | Cooper | 1804 | | M | Supravesical fossa, bilateral | Peritoneal sac covering bladder diverticulum | Long | Reducible | Died, cause unknown |
| 2 | Ring | 1804 | 23 | F | Right supravesical into prevesical space | Strangulated omentum size of a hen's egg | 6 days | Strangulated omentum | Died sixth day; no operation |
| 3 | Linhart | 1856 | | | Supravesical into prevesical space | Small intestine | Asymptomatic | Accidental post-mortem finding | Died from other causes |
| 4 | Havago | 1878 | 58 | M | Right supravesical into prevesical space | Loop of intestine size of walnut | 13 days | Strangulated gangrenous, perforated | Died thirteenth day; no operation |
| 5 | Lupo | 1881 | 50 | M | Right supravesical fossa through transversalis fascia lateral to rectus muscle | Loop of small intestine with hypertrophied walls | Asymptomatic | Incarcerated; incidental post-mortem finding | Died, cause unstated |
| 6 | Aschoff | 1896 | 61 | M | Left supravesical fossa into medial inguinal fossa | Small intestine | 3 days | Strangulated but viable | Recovered after operation |
| 7 | Brentano | 1897 | 45 | M | Left supravesical fossa to prevesical space | 8 cm. of small intestine | 3 days | Strangulated but viable | Recovered after operation |
| 8 | Maydl | 1898 | Old | M | Right supravesical fossa, bilateral | Small intestine in one, fatty tumor in other | Acute | Strangulated intestine | Died without operation |
| 9 | Waldeyer | 1899 | Old | M | Left supravesical fossa to medial inguinal fossa | Mass of omentum size of hazelnut | Asymptomatic | Incidental post-mortem finding | Died, cause unknown |
| 10 | Catani and Gatardoni | 1902 | 60 | M | From supravesical fossa into bladder | Intestinal loop | 1 yr. after blow on abdomen | Strangulated by bladder wall musculature | Died without operation |
| 11 | Blum | 1904 | 23 | M | Left supravesical fossa to prevesical space | Small intestine | 1 yr. | Strangulated | Died without operation |

| 12 | Dall | Arque | 1907 | 36 | M | Left supralesical fossa to prelesical space | Peritoneal sac empty at autopsy | Unknown duration | Reduced spontaneously | Died of other causes |
|----|----------|-------|------|----|---|---|---|-----------------------------------|--|----------------------------------|
| 13 | Jachne | | 1908 | 22 | M | Right supralesical fossa to prelesical space | 20-25 cm. of intestine | 14 days | Strangulated and gangrenous | Lived but fecal fistula remained |
| 14 | Fromme | | 1908 | 39 | M | Left supralesical fossa toward obturator foramen | 10 cm. of small intestine | 14 days | Strangulated | Recovered after operation |
| 15 | Reich | | 1909 | 62 | M | Left supralesical fossa into prelesical space | 10 cm. of small intestine and some incarcerated omentum | 5 days | Strangulated intestine, incarcerated omentum | Died after operation |
| 16 | Reich | | 1909 | 75 | M | Right supralesical fossa toward obturator foramen | 11 cm. of small intestine | 24 days | Strangulated | Died after operation |
| 17 | Traka | | 1913 | 57 | M | Left supralesical fossa to prelesical space | 10 cm. of small intestine | 3 days | Strangulated and gangrenous | Recovered from operation |
| 18 | Shuttze | | 1916 | 34 | M | Right supralesical fossa laterally into inguinal region | Small intestine | 9 wk. of intermittent ileus | Incarcerated intestine | Results not given |
| 19 | Luttmann | | 1919 | 67 | F | Right supralesical fossa to prelesical space | 12 cm. of intestine | 9 mo. chronic, 9 days acutely ill | Strangulated and gangrenous intestine | Recovered after operation |
| 20 | Luttmann | | 1919 | 26 | M | Supralesical fossa toward femoral region | Omentum and diverticulum of bladder | Few months | Incarcerated | Recovered after operation |
| 21 | Bayer | | 1922 | 58 | M | Right supralesical fossa to prelesical space | Small intestine | 3 days | Strangulated and gangrenous intestine | Died after operation |
| 22 | Vogeler | | 1925 | 55 | M | Left supralesical to prelesical space | Small intestine | 2 mo. | Reducible | Recovered after operation |
| 23 | Hahn | | 1925 | 32 | M | Left supralesical to prelesical space | Small intestine | Acute | Strangulated and gangrenous intestine | Died after operation |
| 24 | Schiele | | 1926 | 44 | M | Left supralesical to prelesical space | Loop of lower ileum | 6 days | Incarcerated | Recovered after operation |

TABLE I—CONT'D

| NO. | AUTHOR | DATE | AGE | SEX | LOCATION | CONTENTS OF SAC | DURATION OF SYMPTOMS | TYPE | RESULTS |
|-----|------------------|------|-----|-----|---|--------------------------------------|---|------------------------------------|---------------------------|
| 25 | Kudrnac | 1926 | 25 | M | Center of suprapresical fossa to prevesical space | 20 cm. of gangrenous small intestine | Chronic | Strangulated, gangrenous intestine | Not reported |
| 26 | Kudrnac | 1926 | 46 | F | Suprapresical to paravesical space | 8 cm. of small intestine | Acute | Strangulated, gangrenous intestine | Not reported |
| 27 | Cestmir | 1928 | 26 | M | Suprapresical to prevesical space | 5 cm. of small intestine | 18 hr. | Strangulated | Recovered after operation |
| 28 | Cestmir | 1928 | 53 | M | Left suprapresical to prevesical space | 10 cm. of small intestine | 2 days | Strangulated | Recovered after operation |
| 29 | Watschugoff | 1931 | 24 | M | Left suprapresical to prevesical space | Small intestine | 24 hr. | Strangulated | Recovered after operation |
| 30 | Watschugoff | 1931 | 50 | M | Left suprapresical to prevesical space | 12-15 cm. of intestine | 4 days | Strangulated | Recovered after operation |
| 31 | Watschugoff | 1931 | 29 | M | Suprapresical to prevesical space | Small intestine | 24 hr. | Strangulated | Recovered after operation |
| 32 | Walker | 1933 | 51 | M | Right suprapresical to prevesical space | Small intestine (ileum) | 4 days | Strangulated | Recovered after operation |
| 33 | Walker | 1933 | 63 | M | Right suprapresical to prevesical space | Loop of ileum | 2 days | Strangulated | Recovered after operation |
| 34 | Kochaj and Wolf | 1934 | 65 | F | Left suprapresical to prevesical space | 75 cm. of small intestine | Intermittently for several years; obstruction, 2 days | Strangulated | Recovered after operation |
| 35 | Kochaj and Wolf | 1934 | 62 | M | Right suprapresical to prevesical space | 15 cm. of small intestine | 3 days | Strangulated | Died after operation |
| 36 | Finsterer | 1937 | 75 | M | Right suprapresical to prevesical space | 10 cm. of ileum | 30 hr. | Strangulated intestine, gangrenous | Recovered after operation |
| 37 | Stalker and Gray | 1939 | 61 | M | Right suprapresical to prevesical space | Loop of ileum | 3 days | Strangulated but viable | Recovered after operation |
| 38 | Warvi and Orr | 1940 | 67 | M | Right suprapresical to prevesical space | 10 cm. of ileum | 2 wk. intermittent, 10 days last continuous attack | Strangulated but viable | Died after operation |

the subject since that time. We will not discuss the external types for they do not present important diagnostic or therapeutic problems.

Internal supravescical hernias are rare and difficult to diagnose. Thirty-seven cases have been recorded in the literature completely enough to tabulate essential facts and group them as authentic cases (Table I). Three authors, Szabo,³⁹ Ornatauyan,⁴⁰ and Kramareuko,⁴¹ have been referred to by others as having reported true cases of internal supravescical hernias, but we have been unable to secure their publications for confirmation. Cases have been omitted from the tab-

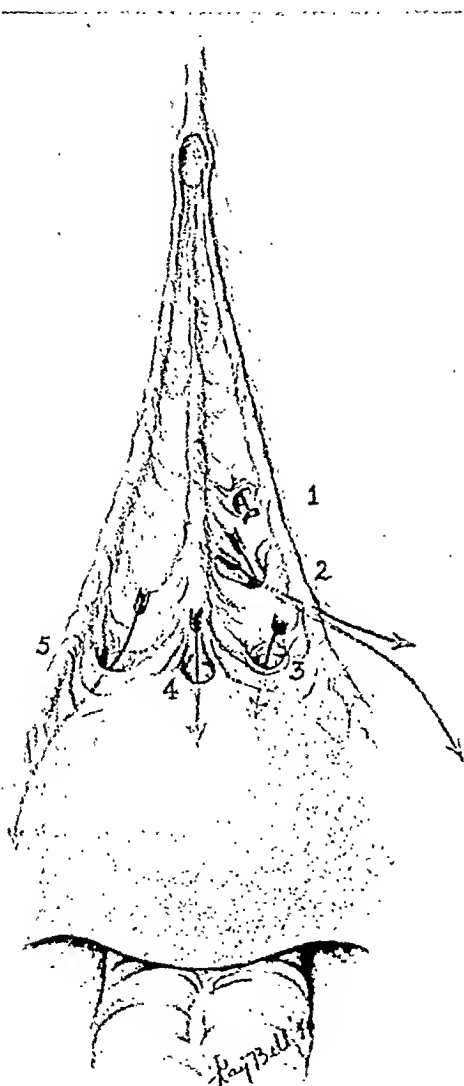


FIG. 2.—Sketch of supravescical fossa showing the five directions in which hernias arising in this fossa generally extend: 1, to hypogastrium (external); 2, to inguinal, femoral or obturator rings (external); 3, to paravesical space; 4, to fundus of bladder; 5, to paravesical space.

ulation of true cases of supravesical hernias because of inadequacy of reports which have left the sites of origin and of the hernias in doubt. These are recorded by Cloquet,⁴² Goyrand,⁴³ Velpeau, Monari,⁴⁴ Santucci,⁴⁵ Hutcheson,⁴⁶ De Grinocoli,⁴⁷ Kostancecki,⁴⁸ Kaufmann, Drandt,⁵ Textor,⁴⁹ Kirchner,⁵⁰ Deus,⁵¹ Foubert,⁵² Trnka,⁵³ Hartung, and Luttelmann. Watschugoff⁵⁴ stated that 16 cases had been reported prior to his article, but he did not give any definite references or details. If these possible cases could be proved and added there would be a total of over 60 cases of internal supravesical hernias recorded in the past. In addition there are 11 cases which have been described with empty internal supravesical hernial pockets to which we have already referred. Watschugoff found 3 internal supravesical hernias in 1,500 hernia operations and estimated that 0.2 per cent of all hernias are of this type.

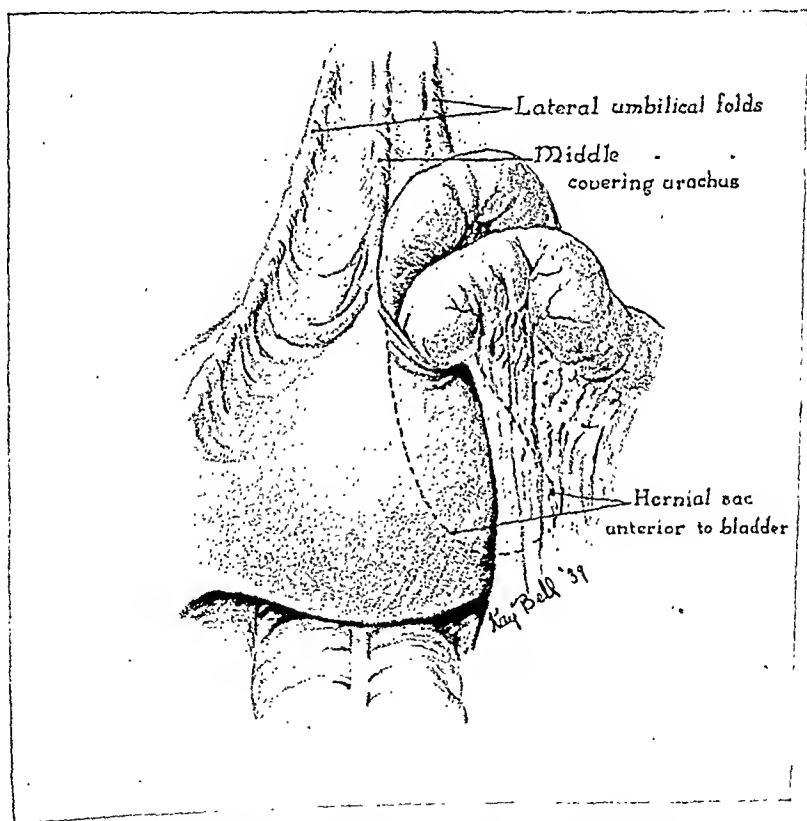


Fig. 3.—This sketch shows location of hernia reported here.

CASE REPORT

We here record an additional case of typical supravesical hernia with an illustration showing its extension into the prevesical space (Fig. 3).

T. S., a male, aged 67 years, was admitted to the University of Kansas Hospitals June 29, 1938. The chief complaints were abdominal pain and vomiting.

The illness began two weeks before admission with generalized cramping pains in the abdomen followed by vomiting. These symptoms persisted for three days and gradually subsided. He was free from symptoms for a week when the acute symptoms recurred. When admitted to the hospital he had been ill four days. During this time he had generalized abdominal pain, more pronounced in the lower abdomen, and persistent vomiting. He was very much prostrated and complained of some palpitation and occasional dyspnea. There was a history of nocturia with some difficulty in starting the urinary stream.

He appeared acutely ill and was obviously very weak. There was some abdominal distention and abdominal tenderness. The tenderness was chiefly confined to the lower abdomen. The inguinal rings were enlarged, but a hernia could not be found. The prostate was enlarged and somewhat tender. He had 125 c.c. of residual urine. A scout film of the abdomen, taken the morning after admission, showed a small amount of gas in three short coils of the small intestine. The second day a barium enema revealed nothing of pathologic importance except diverticula.

The morning following admission the blood chemistry showed a nonprotein nitrogen of 115 mg.; creatinine, 4.4 mg.; and chlorides, 270 mg. per 100 c.c. of whole blood. The red and white blood counts were within normal limits. There was a trace of albumin and a few pus cells in the urine. Intestinal obstruction was suspected, but, because of the blood chemistry findings, uremia was considered a possible cause of the abdominal distention. After six days' observation and treatment with intravenous dextrose and Ringer's solution, an exploratory abdominal operation was done through a right rectus incision. An opening 2 cm. in diameter was found near the apex of the bladder to the right of the peritoneal fold of the urachus in which was incarcerated a loop of ileum 10 cm. long. The fibrous ring of the opening was enlarged and the bowel easily freed. The bowel was constricted at the ring but still viable. The hernial sac was about 6 cm. long and extended downward in front of the bladder and to the right behind the right conjoined tendon. The sac was freed, removed, and the defect in the peritoneum closed.

The general condition of the patient did not improve following the operation. The abdominal wound disrupted on the fifth postoperative day and death occurred two days later. An autopsy was not permitted. The clinical and x-ray findings were typical of bronchopneumonia.

DIAGNOSIS

Walker, Stalker and Gray⁵⁵ and others state that a definite preoperative diagnosis of internal supravescical hernia has never been made nor do they believe that it will be made in the future. Fromme⁵⁶ did make this diagnosis on the basis of typical clinical findings confirmed by a cystoscopic visualization of a bulging of the anterior bladder wall caused by a prevesical hernia. Weil⁵⁷ states that Draudt is also said to have made the diagnosis preoperatively, but the report of Draudt's case is not complete enough to classify it as a supravescical hernia. Reich and Wildegans⁵⁸ believe it possible to make a correct clinical diagnosis of internal supravescical hernias.

The type of patient usually afflicted with an internal supravescical hernia is a well-nourished male between the ages of 22 and 74 years with a history of having lost some weight before the onset of symptoms.

Symptoms occur only with visceral retention in the internal supravescical hernial sac. They are usually those of acute intestinal obstruc-

tion with small bowel strangulation. Because of the encroachment upon the bladder, urinary symptoms are common. Symptoms that Reich considers pathognomonic are intestinal distention and tenderness directly over the bladder with other manifestations of intestinal obstruction. Because of the advanced age of many patients, bladder symptoms may be interpreted erroneously as being due to disease of the prostate.

In making a diagnosis the signs and symptoms of acute intestinal obstruction are readily interpreted. A scout film is a diagnostic aid. A cystoscopic examination of the bladder may be made for evidence of pressure deformity if the condition of the patient will permit. Tenderness in the bladder region with symptoms of acute bowel obstruction suggests the possibility of strangulation in the bladder area. Very frequently the serious condition of the patient will make prolonged and repeated examinations dangerous.

TREATMENT AND PROGNOSIS

The treatment is that of acute intestinal obstruction with strangulation. The necessity of intestinal resection increases morbidity and mortality. It is usually not advisable to free the sac in this type of hernia for the patient may not tolerate extensive surgery and removal of the sac does not improve the results. Most authors advise simple freshening of the edges of the hernial sac and closing it with a continuous suture with an added covering of the peritoneal fold most accessible. Reexpansion of the urinary bladder soon obliterates the space previously occupied by the hernia.

Of the 34 cases in Table I with known results there were 15 deaths, or a mortality rate of 44.1 per cent.

SUMMARY AND CONCLUSIONS

Etiologic factors and pathogenesis of internal supravescical hernias are discussed with a description of the anatomy of the supravescical fossa.

A review of the nomenclature has shown that at least twenty-two different terms have been used in describing the various types of internal supravescical hernias. "Supravescical hernia" has been chosen as the most satisfactory general term for hernias arising in the supravescical fossa. Modifying terms to indicate the origin and location of the various types of supravescical hernias may be used without confusion. Five possible directions of herniation from the supravescical fossa are described and illustrated.

At least 60 cases of internal hernias occurring in the region of the bladder are reviewed and of these 37 have been reported completely enough to be tabulated as true supravescical hernias. The remainder are considered doubtful cases.

An additional case of internal supravescical hernia of the prevesical type is reported. A preoperative diagnosis of intestinal obstruction of unknown cause was made. The diagnosis was obscured by symptoms of uremia and by lack of typical early x-ray evidence of small bowel obstruction. It is possible that the obstruction was not complete during the patient's first few days in the hospital.

The diagnosis of internal supravescical hernia is possible preoperatively if the symptoms and signs of intestinal obstruction with strangulation, urinary disturbance, and cystoscopic visualization of a protrusion of the anterior bladder are found associated.

The treatment is that of acute intestinal obstruction with strangulation plus simple closure of the hernial sac. The results of treatment depend upon the early recognition of the condition and prompt adequate therapy.

The mortality rate of reported cases has been 44.1 per cent.

We believe that all hernias arising in the supravescical fossa should be called supravescical hernias. The exact type of supravescical hernia may have the additional designation of external or internal. The external type passes either directly through the anterior abdominal wall or indirectly through inguinal, femoral, or obturator openings. The internal type may have prevesical, paravesical, intravesical, or lateral pelvic locations. Hernias extending to the region of the bladder, but arising outside of the supravescical fossa, should be classed according to their points of origin.

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good⁴ and Taylor,⁵ constantly reported throughout the years modifications of his operative procedure based on follow-up examinations of patients operated upon according to his method.

In 1903, after fourteen years, the number of patients so operated upon came to over 1,000. It is interesting to speculate not only as to the total number of patients that have had the Halsted operation for the radical cure of hernia performed upon them either by those who were trained on his staff or indirectly trained in his method and technique by one of his former assistants, but also as to the percentage of cures obtained by this procedure.

In one of his later contributions Halsted,² after having emphasized the advantage of employing the cremasteric muscle and fascia as well as the possibility of turning back a flap of the aponeurosis over the rectus muscle, as a support to the lower angle of the wound in closing, goes on to state: "The future will decide these nicer points, and it would seem that only the nicer points remain now to interest the operator." It is the purpose of this paper to call attention to one of these "nicer points" or which more appropriately may be called major points that has been found useful not only in the more difficult, but also in the large majority of cases of inguinal hernia; i.e., the employment of the fascia overlying the rectus abdominis muscle in order to close a defect in the lower inguinal region caused by a deficiency of the conjoined tendon.

In the early days of the development of the operation for the cure of inguinal hernia, attention was directed mainly to the spermatic cord and thus to the upper angle of the wound. The cord was felt to be the first cause of the hernia and the main obstacle to its cure. The lower angle of the wound was not considered of as great importance as the upper. Although the truth of the liability of the spermatic cord is not to be doubted, the weakness of the lower inguinal region might be more properly ascribed to developmental defects in the fascia concomitant with the descent of the testis rather than to the presence of the spermatic cord. This point has received support in the now-recognized lack of necessity of transplanting the cord for the successful operative cure of inguinal hernia and has emphasized the importance of proper tissue support of the hernial hiatus in the abdominal wall. As long ago as 1896 recurrences at the lower angle of the wound were recognized by Bloodgood⁴ as being frequent, and through the years up to the present time it would seem that Bloodgood's observations have been confirmed; i.e., that the majority of hernias recurred in the lower weak area. One of the most important of the facts ascribed to Bloodgood was the great variation in the width of the conjoined tendon and the responsibility of the insufficient tendon for the recurrences at the lower angle of the wound, through the external ring, directly. In 1892 Wölfler⁶ described a method of strengthening this area by using

THE USE OF THE RECTUS FASCIA FOR CLOSURE OF THE LOWER OR CRITICAL ANGLE OF THE WOUND IN THE REPAIR OF INGUINAL HERNIA

WILLIAM FRANCIS RIENHOFF, JR., M.D., BALTIMORE, MD.

(From the Department of Anatomy and Surgery, Johns Hopkins University)

SINCE the sixteenth century when Pierre Franco, an ordinary rupturer and stone cutter, first relieved incarceration by herniotomy, this operation has been of vital interest to surgeons. However, even earlier references¹ to various operations and other methods employed in the treatment of hernia may be found in the writings of Celsus, Heliodorus, and Paul of Aegina. According to Albert,¹ from the Middle Ages to the introduction of antiseptic surgery various methods have been in vogue and were classified by him as follows: (1) pressure with or without the simultaneous application of irritating and so-called contracting remedies; (2) caustics and the actual cautery; (3) ligature of the sac with or without cutting it off; (4) introduction of foreign bodies into the hernial sac; (5) the injection of irritating fluids within or outside of the hernial sac; (6) subcutaneous suture. Most of these methods are still practiced, and, in spite of the fact that the operative treatment of hernia has been well established for many years, the rebirth of the ancient and discarded method of injection has only recently appeared in the literature. The obvious lack of unanimity of opinion in regard to the operative or nonoperative method of treatment is based upon the fact that in a certain number of patients, although this be a small percentage, operation has failed to bring about a cure of the hernia. There are always, of course, those patients who either refuse to subject themselves to an operation because of fear or who are properly advised against such a course because of some concurrent complications. The most cursory review of the literature will reveal that each year publications on the operative treatment of this affection have been made, thus indicating that, in spite of the fact that the majority of inguinal ruptures are now easily and permanently cured by a variety of procedures and by the average operator, nevertheless, there are a small, but definite, minority of instances in which recurrence is all too common. The underlying surgical principles upon which an operative cure of hernia is based completely baffled the efforts of the best surgeons for years and it was not until the totally independent publications of Halsted² and Bassini³ that the surgical technique was placed on a rational basis. Although after his original contribution in 1890, Bassini made no further reports, Halsted,² either directly or through one of his associates, notably Blood-

rectus muscle to be used in the presence of a defective conjoined tendon. Fig. 4 is a drawing by Brödel from a sketch made at the time of Halsted's operation by Harvey Cushing.

This procedure of necessity leaves a weak area along the lateral border of the rectus muscle through which herniation has occurred in the past; besides, the flap of the fascia was placed beneath the spermatic cord. Although at times very useful, this method has not been popular. Halsted² mentioned relaxation incisions higher up on the rectus muscle in order to loosen the internal oblique so that this muscle might be more readily sewn to a lower level along Poupart's ligament, but he was careful to advise against the employment of relaxation incisions lower down on the rectus because, if it were found desirable to turn back a flap in this region, such incisions might interfere.

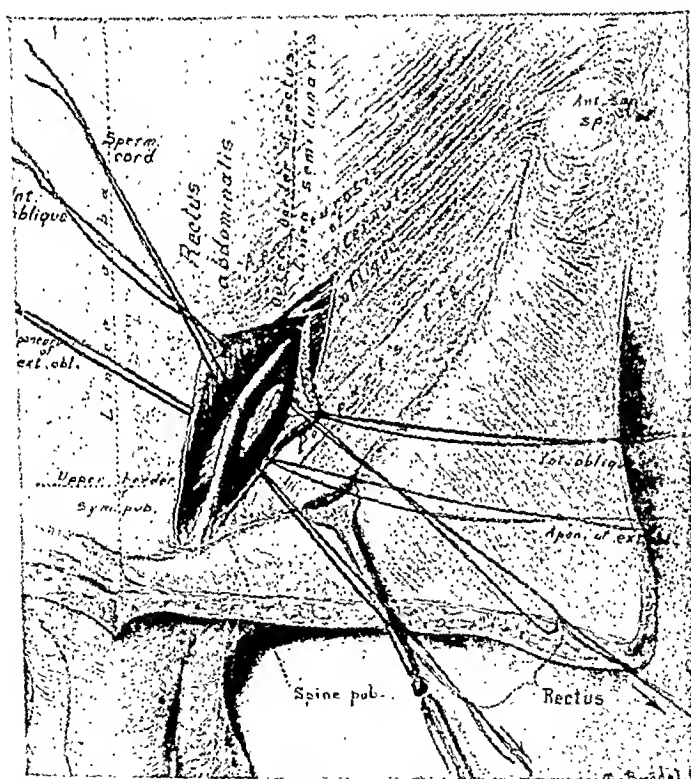


Fig. 2.—The method of transplanting the rectus muscle. The sac has been excised and peritoneal cavity closed; internal oblique muscle has been divided, the rectus exposed and transplanted; at this stage the wound is ready for deep sutures. This drawing shows how perfectly the transplanted rectus muscle lines the lower half of the wound. (From Bloodgood, J. C.: Operations on 459 Cases of Hernia in the Johns Hopkins Hospital From June, 1889, to January, 1899, Rep. Johns Hopkins Hosp. 7: 223-563, 1899.)

Dissections in over 200 cadavers without hernias, performed in the course in surgical anatomy, in addition to experience at the time of operations for hernia called our attention to the fact that the difficulty

the lower end of the rectus muscle, but according to his description and the diagram, published by Bloodgood (Fig. 1), the rectus muscle with its fascial covering was drawn laterally under considerable tension and was attached to only the middle third of the inguinal ligament. The inner lower angle, therefore, was not supported by this procedure.

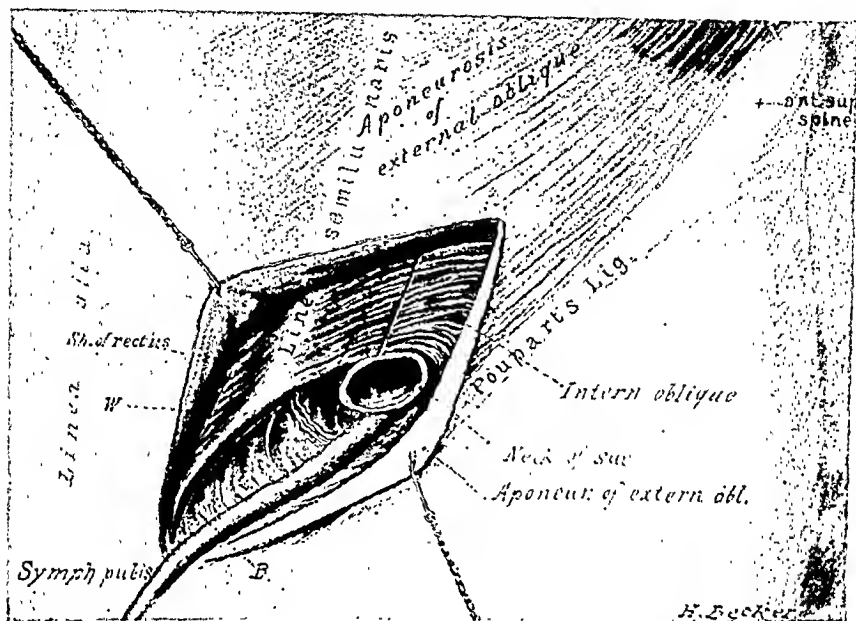


Fig. 1.—The anatomy of the inguinal canal. The straight line on the internal oblique muscle represents the correct direction and extent of its division. The dotted lines represent the direction and position which should be avoided in dividing the muscle. W, The direction and extent of the division of the anterior sheath of the rectus in Wölfler's method; B, the direction and extent of the division of the fascia to expose the rectus muscle in the writer's method; also, the extent of the conjoined tendon if it is wide and firm; if it is obliterated the transplanted rectus muscle covers this portion of the inguinal canal. (From Bloodgood, J. C.: Operations on 459 Cases of Hernia in the Johns Hopkins Hospital From June, 1889, to January, 1899, Rep. Johns Hopkins Hosp. 7: 223-563, 1899.)

Bloodgood in 1899 also reported the use of the rectus abdominis muscle to fill in the lower angle by incising the lateral margin as shown in Figs. 1-3. This powerful straight muscle gradually pulled away from such a mooring as soon as the patient was up and around. Probably one of the most interesting examples was recently related to me by Follis.⁷ He had performed such a plastic closure on a patient who, shortly after discharge from the hospital, was riding a bicycle up Chase Street in Baltimore when he felt something tear in the lower inguinal region. After this incident he greeted Follis with the remark: "This is the first time I have been able to stand up straight since the operation." On examination there was some ecchymosis in the skin near the lower end of the scar. It was assumed that the transplanted portion of the rectus muscle had torn loose. This procedure was finally given up. Berger⁸ in 1902 and Halsted² in 1903 suggested turning back a flap of the lower end of the fascia covering the

of demonstrating a conjoined tendon or *falx inguinalis* has been very great indeed. Some of the details of the anatomy of the inguinal region, such as the lateral abdominal muscles and their covering fasciae together with Scarpa's and the transversalis fascia, the aponeurosis of the external oblique, and the inguinal or Poupart's ligament, are well understood, but with regard to other structures the fasciae are quite variable and their relationship indistinct. In a normal, well-developed adult, in the dissecting room, the various fascial layers, even in the absence of a hernia, are almost impossible to demonstrate to the students without producing artefacts. How then can one not experienced in such dissections discover at operation and employ for closure of the hernial orifice these structures that in the presence of a hernia and further attenuation are even more indistinct than normally. The result is, of course, a poor closure of the vital lower angle of the wound with inadequate fascia under more or less tension. The fact that the great majority of recurrences are direct hernias is ample proof of the above statement. In fact, in all but children or very young vigorous adults who are neither fat nor emaciated it is impossible, as a rule, to show in a satisfactory manner any form of fascial layer in the lower inguinal region except the aponeurosis of the external oblique and the transversalis fascia lying next to the peritoneum. Most frequently the surgeon or even the anatomist is confronted with the difficult problem arising from an undeveloped or an acquired atrophy of the conjoined tendon, or from fatty degeneration and atrophy of the internal oblique muscle. Again, even in otherwise well-developed young male adults there is not infrequently a marked congenital attenuation of the entire area between the lateral edge of the rectus muscle and the medial margin of the inner abdominal ring. At this latter point it will be recalled a thickening of the fascia of the internal oblique and transversus fascia is termed the ligament of Hesselbach. The fascial sheet of these two muscles continues inferiorly to contribute to the formation of the inguinal or Poupart's ligament and medially to form a part of the abdominal wall covering the so-called weak area or Hesselbach's triangle. Frequently in the interior abdomen the aponeuroses of the obliquus internus and transversus abdominis remain undivided, lateral to the sheath of the rectus, and this undivided or fused part constitutes the conjoined tendon. Although in the superior part of the abdomen the aponeurosis of the transversus muscle forms the posterior sheath of the rectus, while that of the internal oblique splits to straddle the rectus sheath, these relations are changed in the inferior inguinal region. Inferiorly the aponeurosis of the internal oblique, if it is not fused with that of the transversus to form a conjoined tendon, is inserted upon the ventral surface of the rectus sheath. When strongly developed, it is usually separable at the point of insertion from the transversus abdominis, and

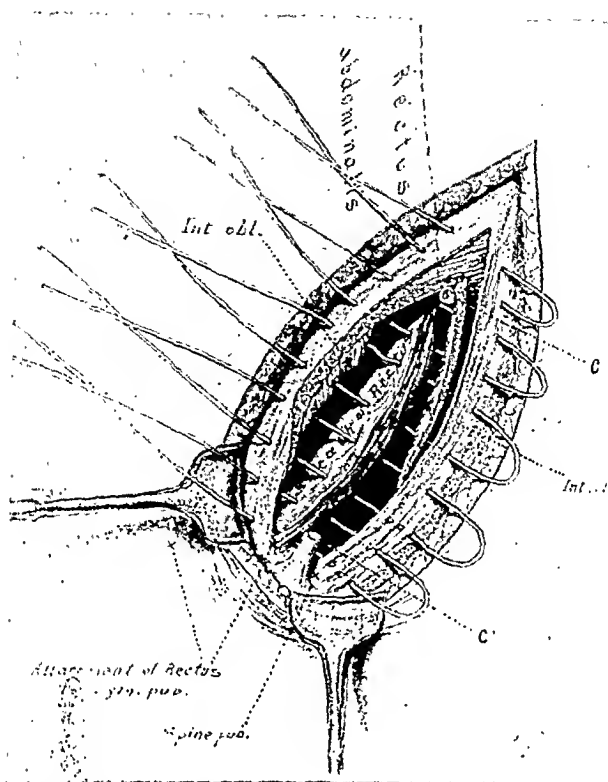


Fig. 3.—The transplanted rectus included by the deep sutures. In this drawing the cord has been excised in order to demonstrate the operation more clearly. (From Bloodgood, J. C.: Operations on 459 Cases of Hernia in the Johns Hopkins Hospital From June, 1889, to January, 1899, Rep. Johns Hopkins Hosp. 7: 223-563, 1899.)

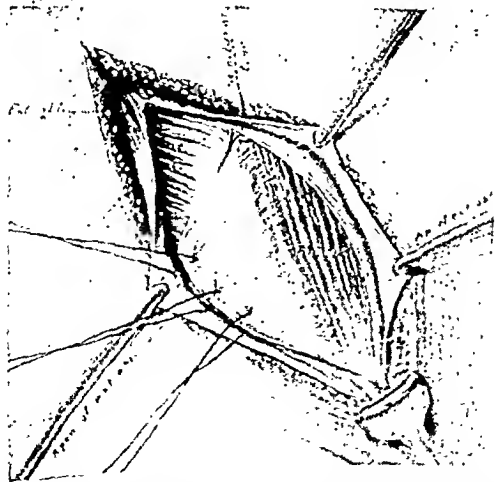


Fig. 4.—Transplantation of triangular flap from anterior sheath of rectus muscle. (From Halsted, W. S.: Bull. Johns Hopkins Hosp. 11: 208-214, 1903.)

lem in the satisfactory closure of a hernia wound. For these reasons a simple and most inviting operative method is suggested which not only augments the fascia present in the lower inguinal region, but at the same time permits of a secure closure without producing the slightest tension and thus remains true to one of the greatest and most fundamental surgical principles.

OPERATIVE TECHNIQUE

The operative method and technique employed are in every way similar to those described by Halsted, with the exception of the manner in which the lower angle of the wound is closed. The most meticulous technique and hemostasis are observed and fine silk sutures are employed routinely throughout the wound in bringing about the repair of the defect in the abdominal wall. Transplantation of the spermatic cord has not been done because it is thought to be unnecessary for the cure of inguinal hernia, either direct or indirect. In fact, the cord with its cremasteric muscle and fascia is felt to be a valuable addition of tissue to augment the paucity existing in the lower angle of the wound.

A careful sharp dissection of the hernial sac down to peritoneum, with only the slightest extraperitoneal tissue remaining, is felt to be desirable. Ligation with transfixion sutures of the sac as high up as possible is undoubtedly one of the more important steps in the operation. The stump of the neck of the sac should be allowed to retract freely under the edge of the lower margin of the internal oblique and transversalis muscles. Fixation of this stump to the latter muscles, practiced by some, is to be condemned, for a funnel-like pouch of peritoneum is formed at the site of fixation and may be the starting point of a new hernia. Closure of the neck of the sac, if large, may be equally well accomplished by an internal purse-string suture. On the left side, when a sliding hernia is encountered which interferes with a high dissection of the peritoneum due to the position of the sigmoid colon, a series of external purse-string sutures may be employed to advantage. In this manner the neck of the sac, the area of adjacent peritoneum, and the colon are protruded into the peritoneal cavity by such a series of purse-string sutures laid in a pattern of circles of ever-increasing diameter. Three such sutures are, as a rule, sufficient. High ligation of the sac can be accomplished only if the sac is carefully and completely freed from the tissue surrounding it.

As shown in Fig. 5, the incision is made on an oblique line, beginning about one fingerbreadth inside and below the anterior superior spine of the ilium and crossing down to a point approximately over the external inguinal ring about one fingerbreadth external to the spine of the pubis. A similar incision is made in the aponeurosis of the external oblique muscle along the course of its fibers for the same length as the skin incision. This incision is made so that the external inguinal ring

in the absence of a fusion with the latter or of a conjoined tendon, this part of the aponeurosis of the internal oblique forms an aponeurotic arch above with the spermatic cord, the medial part of which constitutes the *falx inguinalis*. Inferiorly the aponeurosis of the transversus inserts on the lateral border of the rectus sheath when the conjoined tendon is absent. Near the inguinal ligament the internal oblique and transversus abdominis are quite similar in that their muscle fibers arise from the lateral part of the ligament, both having fascial attachment to the ligament throughout its entire length.

In summary, it is very rarely true that a fusion of the aponeurosis of the transversus and obliquus internus, thus forming the conjoined tendon, occurs as far lateral as the internal inguinal ring, and in the average adult it is infrequent that this fusion can be found to occur for any practical distance lateral to the attachment of the conjoined tendon to the lateral edge of the rectus sheath. It is more frequent in the dissecting and operating rooms to find the internal oblique muscle and its aponeurosis the more strongly developed of the two and inserting separately on the ventral sheath of the rectus muscle. The *falx inguinalis*, in the absence of a conjoined tendon, is usually contributed to mainly by the aponeurosis of the internal oblique. The weakness or strength of the lower inguinal region is therefore in direct proportion to the strength of the aponeurosis of the internal oblique and transversus muscles between the internal inguinal ring and the lateral edge of the rectus sheath. If they are fused, the structure should be termed the conjoined tendon, which may be strong or attenuated in young or old. An accentuation of the lateral portion near the internal inguinal ring has been termed the *ligamentum interfoveolare* or ligament of Hesselbach, the main function of which appears to be to turn the direction of the spermatic cord. An accentuation of the medial portion has been properly called conjoined tendon, the fibers of which run to the pubis. If the aponeurosis of the internal oblique and transversus muscles are not fused, the conjoined tendon is absent, but the sickle-shaped band of fibers in the accentuated aponeurosis of the internal oblique muscle, the *falx inguinalis*, however, may be and usually is present and definable. The presence or absence of a conjoined tendon, therefore, has nothing whatever to do with the strength or weakness of the lower inguinal fasciae.

In the adult cadavers and operative cases examined, the internal oblique and transversus muscles together in the great majority of instances have been found to be atrophic, indefinite, and attenuated, rather than definite, strong, and readily demonstrable.

It would appear in an as yet incomplete follow-up of cases operated upon for hernias that the lower inguinal region is probably the most vulnerable point for a recurrence of the hernia, whether primarily direct or indirect hernia, and unquestionably offers the greatest prob-

continued as far as the reflection of the aponeurosis of the external oblique will permit. This incision releases the anterior sheath and the enclosed muscles tend to bulge immediately. Lateral displacement of the rectus sheath is then accomplished with the greatest ease and closure of the hernial wound is carried out in close accordance with Halsted's technique.

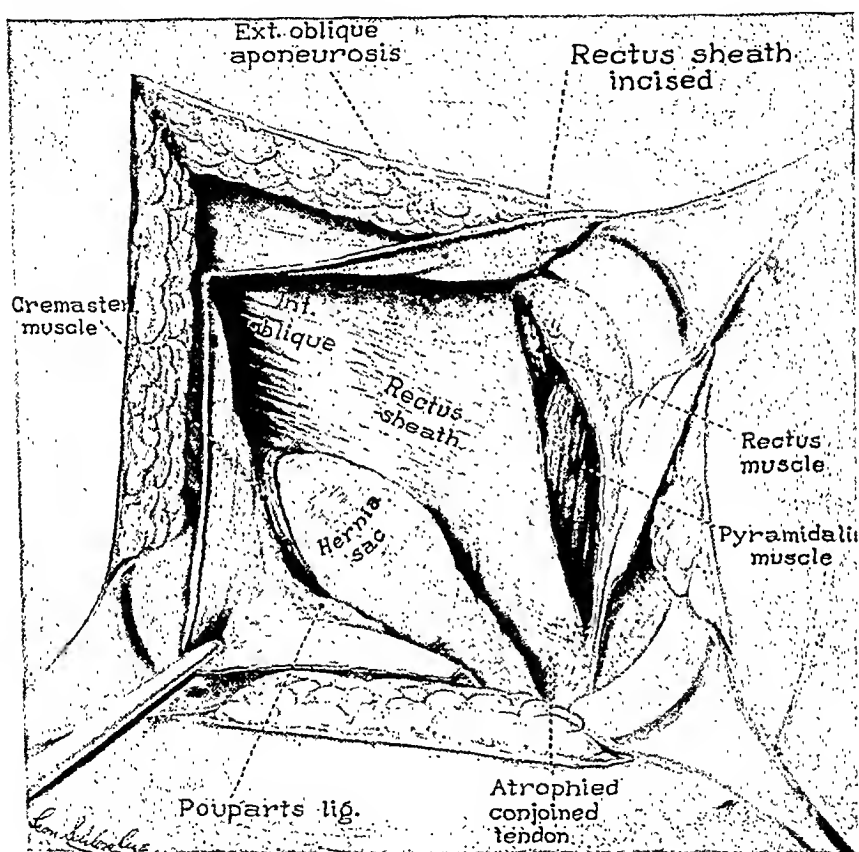


Fig. 6.

As shown in Fig. 7, the cremasteric muscle and fascia are sutured with mattress sutures of fine silk to the undersurface of the lower edge of the internal oblique and transversalis muscles and their aponeuroses, together with the lateral portion of the fascia of the rectus sheath. It will be noted that the spermatic cord is left undisturbed and furthermore that the cremasteric muscle is sutured in such a way that the edge of the aponeurosis of the internal oblique and transversalis muscles, as well as the lateral portion of the rectus sheath, is everted in somewhat of a roll, forming an edge which may be snugly approximated to the inner surface of Poupart's ligament. The cremasteric muscle and fascia not only furnish a strong addition to the tissue closing this

is divided near its upper middle angle. Care must be exercised in dividing the external inguinal ring not to injure the ilioinguinal nerve. It is for this reason that the ring is divided in its most medial portion. As shown in Fig. 5, the aponeurosis of the external oblique is dissected medially as far as possible from the anterior sheath of the rectus muscle. This dissection is carried well past the linea semilunaris toward the mid-line, and, depending on the shape of the abdomen, the aponeurosis of the external oblique can easily be freed to within a few centimeters of the linea alba, thus exposing more than the lateral half of the anterior surface of the rectus sheath and its contained muscle.

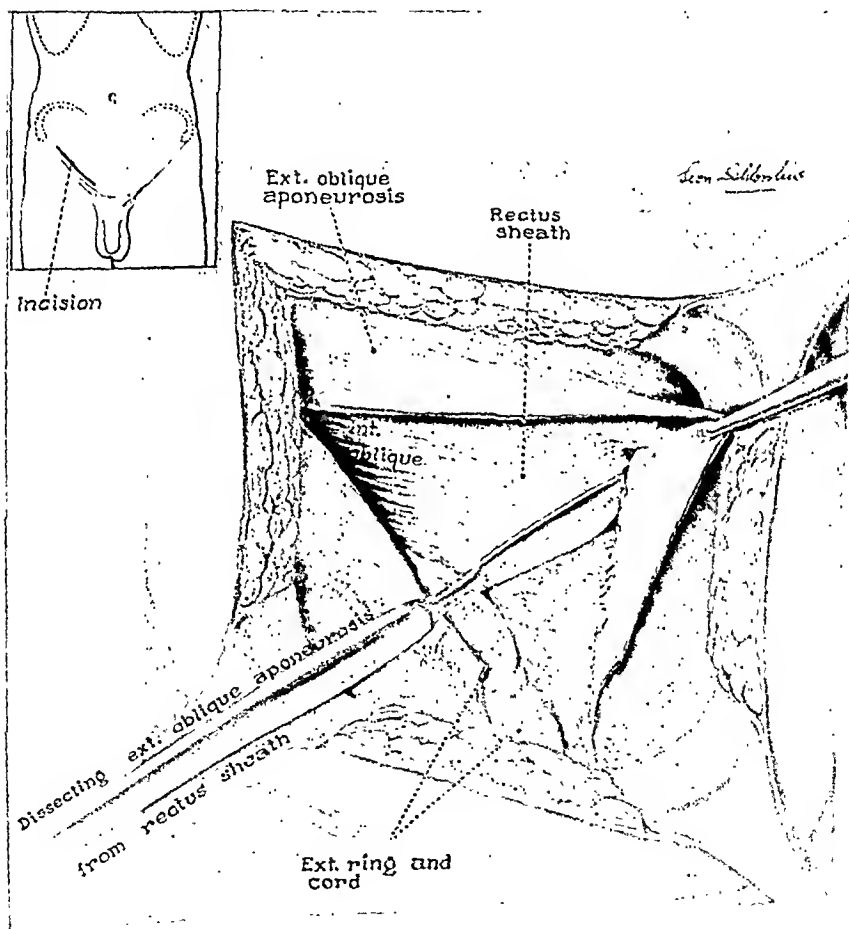


FIG. 5.

A vertical incision is then made through the anterior sheath of the rectus, exposing the pyramidalis muscle and also a portion of the rectus muscle just above its insertion into the pubic bone, posterior to the pyramidalis muscle (Fig. 6). The incision in the rectus sheath is carried down to the superior ramus of the pubic bone and superiorly it may be

effectiveness of the closure when the anterior sheath of the rectus muscle is incised and displaced laterally is quite striking. The hiatus in the anterior sheath is rapidly reformed by the growth of the fascia. The disagreeable features associated with turning out a flap of the rectus muscle are thus avoided for there is no resulting weakness at the lateral edge of the rectus nor is there any permanent defect in the

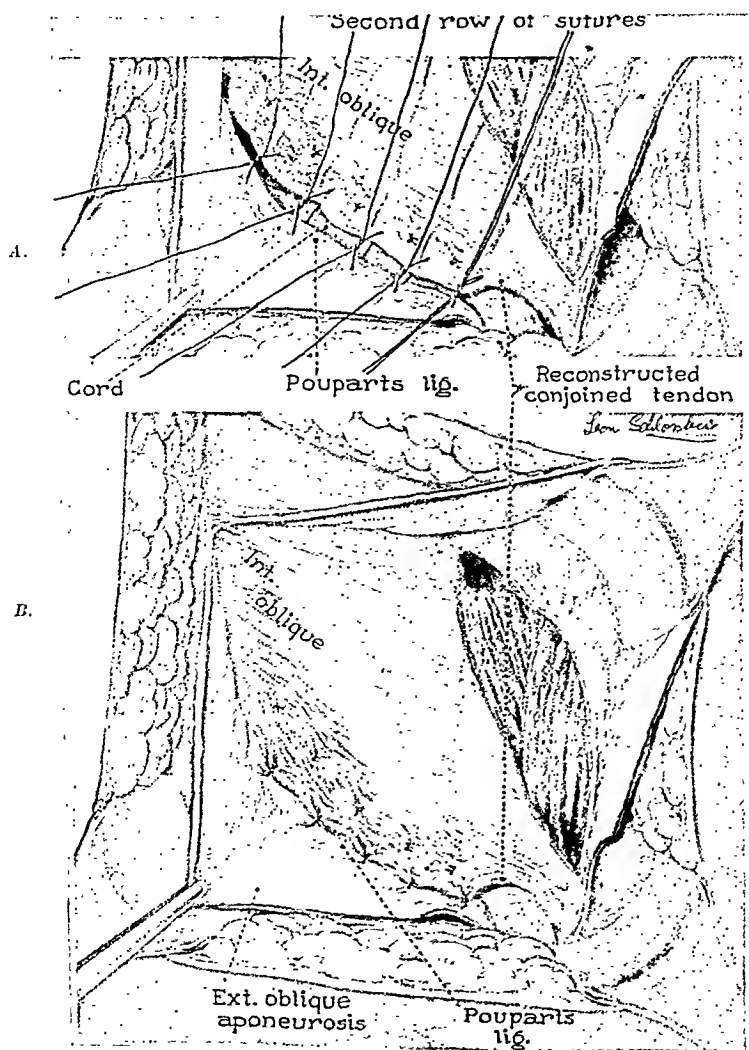


Fig. 8.

sheath of the rectus. A most secure closure of the lower critical angle is thus obtained in the simplest manner and one that is now routinely employed in all inguinal hernias, regardless of the degree of conjoint tendon present or the amount of fascia in this region, rather inadequately described as the weak area, the triangle of Hesselbach, or the lower angle of the wound.

critical angle of the hernial wound, but also serve to obliterate any dead space which might occur after the removal of the hernia.

Fig. 8A demonstrates the suturing of this everted edge of the sheath of the rectus and aponeurosis of the internal oblique and transversalis muscles to the inner surface of Poupart's ligament. These sutures consist of interrupted medium C silk, a double one being used for the final stitch. It is likely that fine silk might be used here because, due to the lateral displacement of the rectus sheath, there is absolutely no tension exerted in obtaining the most complete closure of the hernial wound in its superior, as well as in its inferior, portion. The lower sutures take in not only the lateral margins of the sheath of the rectus, but also whatever other fascia is present in the form of either conjoined tendon, or remnants of it, as well as the falx inguinalis in the event the conjoined tendon is absent.

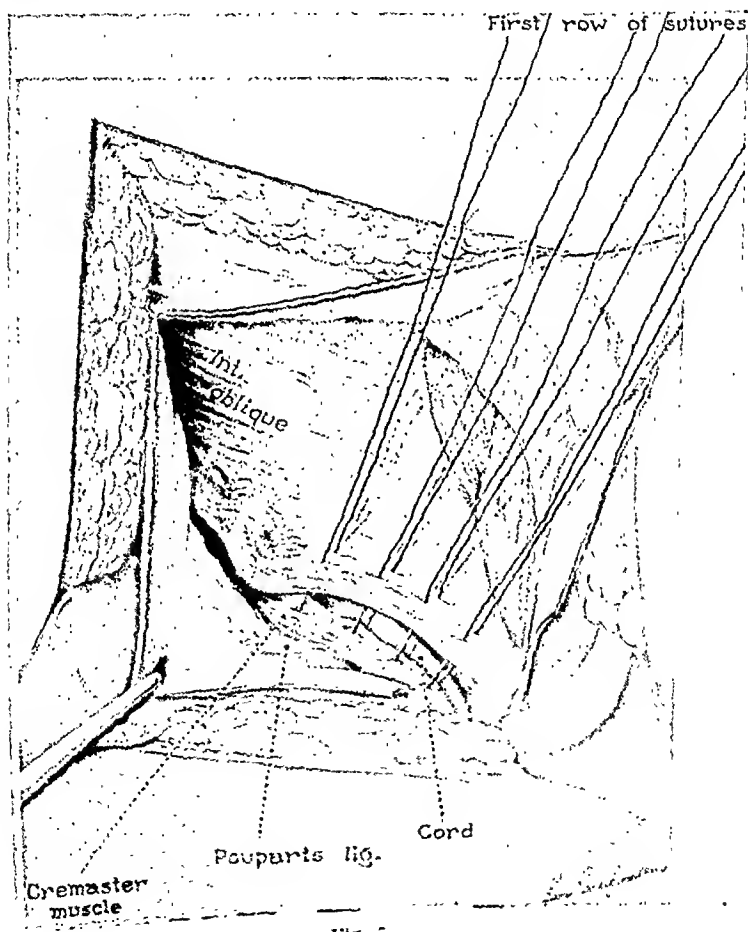


FIG. 7.

Fig. 8B represents the sutures shown in Fig. 8A tied, as well as the sutures holding the cremasteric muscle and fascia. The facility and

forms a stronger abdominal wall than would occur in the mere apposition of the incised edges, but also permits of a broader approximation of surfaces and thus more secure healing. Scarpa's fascia is then brought together with interrupted fine silk sutures and the skin is closed in a similar manner.

There do not seem to be any objectionable features to this procedure and it is of the greatest comfort to the operator to be able in a simple but efficacious manner to employ such an inviting and natural procedure. The question of any tension is immediately done away with in the closure of the fascia over the lower angle. In this manner it is felt that the percentage of recurrences of a hernia in the lower angle of the wound will be very much reduced.

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The overlapping of the middle and lateral flaps of the aponeurosis of the external oblique is then accomplished, as shown in Fig. 9A and B. Interrupted mattress sutures of fine silk are so placed that the lateral flap is tacked to the inner surface of the middle flap and the edge of the middle flap is then sewn down to the anterior surface of the lateral flap. This imbrocation of the aponeurosis of the internal oblique not only

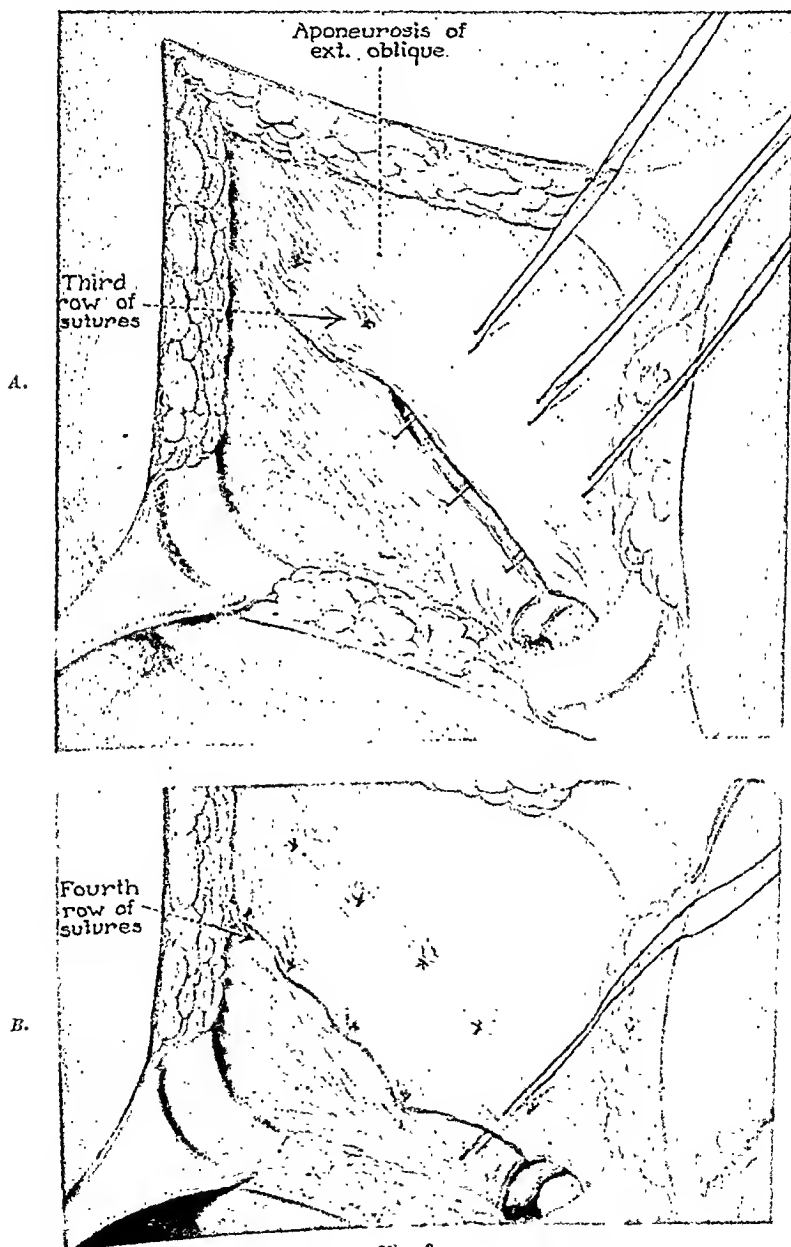


FIG. 9.

been able to find at least a scar and a bit of history strongly suggestive of a cured epithelioma.

In the foregoing, in the event that we have overlooked some essential modifying element belonging to the above problem, it might be helpful if those denying the propriety of prophylactic gland removal after destruction of even a high-grade lip cancer would publish more generous



Fig. 1.—Illustrating squamous-cell node metastases from a basal cell primary growth. *History:* Patient aged 68 years. The ear canal lesion had been growing slowly for several years and patient was referred for treatment because of some recent hemorrhages. *Findings:* This patient had an ulcerated, clinically and microscopically, basal-cell primary growth in and about the ear canal, with a large mass of typical, microscopically positive squamous metastases to the glands in the upper neck. *Treatment:* Complete right-side neck dissection and deep destruction of the primary growth and underlying bone by cherry hot soldering irons.

records of five-year follow-ups and microscopic findings upon which convincing conclusions might be based. This is not meant as a challenge but simply a request for information to which we have not had satisfactory access. We personally see too few early lip cancers to make our results of any statistical value, but, whether few or many, their usually slow onset and insignificant appearance in that stage often fail to impress the patient and this makes a post-treatment follow-up more difficult than in other mouth epitheliomas.

CURRENT TREATMENT OF CANCER OF THE LIP

A CLINICAL SPECULATION

VILRAY P. BLAIR, M.D., AND LOUIS T. BYARS, M.D., ST. LOUIS, MO.

AN UNDERSTANDING surgeon never thinks of squamous-cell or adenomatous cancer as disassociated from potential lymphatic metastasis, and we are finding that even presumed or proved basal cell growths are not necessarily above suspicion (Figs. 1-3). The supposedly relative infrequency of gland involvement from squamous-lip cancer is of itself no sufficient warrant for ignoring its possible occurrence in any individual case. The old surgical estimate was that 70 per cent of squamous-cell epitheliomas of the lip are cured by any type of local treatment that completely controls the primary focus. It is possible that, if the men who are content to treat only the primary lip lesion were able to follow the majority of these patients for a period of five or ten years, the above percentage of lymphatic immunity might prove to be reduced materially. Right or wrong, many present-day radiotherapists deem prophylactic cervical gland dissection as being unnecessary or even harmful after proper radiation of the primary lip growth. This is a vital issue and it might help to clarify the discussion or speculation if the known and unknown factors which their premise must compass be here marshalled and discussed in one group.

There can be no question of a cancer-free interval of varying length between maturity of a primary squamous epithelioma and the occurrence of regional gland contamination, and, if within this absolutely gland-free interval the primary growth were destroyed, the patient will have been cured without surgical invasion of the neck. However, at present we have no way of recognizing just when gland contamination, which is the termination of the free interval, does actually take place. The first clinical characteristic of lymphatic gland metastasis is enlargement of a node, but of necessity there must have been a further lapse of time between contamination of the node and its becoming palpable. This second period, antedating recognizable metastasis, for all we know might be very brief, but from occasional instances of late cervical metastases developing long after destruction of the primary lesion we must conclude that the quiescent period can be prolonged indefinitely, the cancer material apparently remaining dormant within the node for months or years. In cases of this type under our own observation the quiescent period has varied from several months to thirteen years (Figs. 4 and 5). This is not a new observation: Butlin, some thirty-five or forty years ago, recorded similar behavior of the nodes following tongue amputations. Treves cites certain deep squamous-cell neck cancers which he regarded as arising from branchial cleft rests. Our first case of the kind came to us about thirty years ago and in almost all cases we have

been able to find at least a scar and a bit of history strongly suggestive of a cured epithelioma.

In the foregoing, in the event that we have overlooked some essential modifying element belonging to the above problem, it might be helpful if those denying the propriety of prophylactic gland removal after destruction of even a high-grade lip cancer would publish more generous



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Disregarding the comparative intrinsic value of radiation versus excision or mass destruction in the treatment of early or moderately advanced squamous epitheliomas of the lower lip, present public opinion gives a better break to radiation than to surgery on the time-of-treatment factor, and this is the greatest advantage that could be asked. The average patient seeking treatment by a regular medical practitioner is much more apt to choose radiation, which conforms to the widely publicized slogan, treatment or cure "without knife or cautery," than he is to have a sizable piece cut or burned from his own precious lip.



Fig. 2.—Illustrating cervical node involvement from a chronic skin ulceration on the nose. *History:* For several years the patient had a "sore" which was described as an ulceration, not as a wart, on the nose, and about a year before our examination he had noticed the submaxillary enlargement which continued to grow. A few months after this node enlargement, the nose lesion was destroyed with "caustic." *Findings:* The nose lesion had healed with scarring and two perforations through the alar cartilages. A fixed mass of ulcerating glands in the submaxillary region was clinically and microscopically squamous-cell cancer.

Therefore, wisely used radiation has the better chance of eliminating the primary growth before cancer material overcomes the node's resistance than has local surgery. From the strides radiotherapy has made in the past two decades, it seems not unreasonable to hope that sooner or later this or some other selective agent may ultimately supersede mass destruction of even cancerous lymph nodes—"A consummation devoutly to be wished"—but we must deal with present facilities.

Granted positive instances in which a contaminated node has retarded metastases for several years, can we deny either that the nodes in any treated case might have already been contaminated or that there can be unrecognized instances in which the invaded gland totally destroys the contamination? If the latter does happen, it but increases the uncertainty as to how often or how early a purely transient gland contamination actually does occur.



Fig. 5.—Illustrating either dormant sequestration of cancer material or retarded development of a true metastasis within a cervical node, coming from a lip epithelioma. *History:* A 38-year-old plumber burned the lower lip with a splash of hot lead. The wound was indolent for a year, then healed after use of caustic; radium was applied to an "abscess" three years later. *Findings:* Two years after the radium treatment, fissure perforation occurred across lower lip with rough borders. He had at this time a hard right buccal or submaxillary node. *Treatment:* Wide excision of borders of lip perforation and repair with sliding cheek flaps was performed. Neck dissection of the submaxillary node, treatment, and mandible of that side. Patient did not return until eight years later, when he had a wide involvement of the submaxillary node. *Treatment:* Allowed. *Later Findings:* Patient did not return until eight years later, when he had a wide involvement of the submaxillary node. *Treatment:* Allowed.

A shows the type of cancer destruction of the mandible which we have found typical of an extension to the bone from a buccal or submaxillary lymph node. On the postoperative microscope examination the tissue from the rough borders of the treated lip fissure were reported "inflammation," but on re-examination it was found to contain squamous cancer. The gland and cheek tissue removed eight years later was also squamous-cell cancer.

B shows the type of cancer destruction of the mandible which we have found typical of an extension to the bone from a buccal or submaxillary lymph node. On the postoperative microscope examination the tissue from the rough borders of the treated lip fissure were reported "inflammation," but on re-examination it was found to contain squamous cancer. The gland and cheek tissue removed eight years later was also squamous-cell cancer.

suggesting that it is as effective as an early, properly performed excision, there are many circumstances which can render x-radiation the more appropriate, dictated by the stage of the disease, the condition of the patient, or his wishes. However, neither logic nor clinical experience justifies certain recommended unsurgical diagnostic procedures that risk crippling gland resistance without compensatory gain for the patient. Negative findings from suction needling or the use of a punch on a suspected gland are not of sufficient weight to warrant the employment of either; positive ones only confirm what we at present prefer to take for granted. Biopsies are not often necessary for diagnosing any but very early lip lesions, but we use them rather routinely for checking both the diagnosis and the grading of the primary lesion, per-



Fig. 4.—Illustrating squamous-cell buccal node metastasis years after the control of a lip epithelioma. *History:* Patient 76 years of age. Eleven years previously a "cancer" on the lower right lip had been controlled with surface radium. He has had recent right submaxillary growth and ulceration. *Findings:* Patient had keratotic skin on hands and face and showed a well-healed lip scar. He had a fungating mass approximately 4 by 5 cm. on right lower cheek and submaxillary with deep induration, but roentgenogram did not show bone erosion. The buccal gland was enlarged but no lower glands were felt. *Treatment:* Under deep block anesthesia, twelve 12.5 mg. needles and two 10 mg. needles of radium were implanted in various places in and around the area, giving a total dose of 2,730 m.r. hr. Death occurred ten months later. Growth was not controlled.

forming a biopsy of a gland only when the suspected original lesion has been previously eliminated. The proper interpretation of the biopsy picture is most important. A positive diagnosis of epithelial malignancy in all probability will be correct, but a negative microscopic diagnosis that controverts a positive clinical picture of cancer should be regarded with at least grave suspicion. We have long been of the belief that under the above circumstances, in the final analysis, the patient should be given the benefit of the doubt by treating the condition as cancer. We, ourselves, have had few occasions to make such a decision because usually a recheck or another specimen has settled the matter, but we

1. Early removal and microscopic examination of all possibly precancerous lesions or a cautery-biopsy examination of the more advanced. The first will prevent many cancers; the latter will be of great help in planning treatment of the case in hand.

2. Proper attention to possible involvement of the cervical lymphatics.

3. Mindfulness of the fact that death from cancer of the lip or mouth is one of the most terrible ordeals to which human flesh is heir.

There are five accepted facts upon which the intelligent surgical treatment of epithelial cancer is based:

1. If the cancer is completely removed before dissemination occurs, the patient is cured as far as this particular growth is concerned, but this does not eliminate the possibility of the development of some other independent focus.

2. Metastasis occurs chiefly through the lymphatic vessels to the related lymph nodes.

3. The lymph nodes are agencies of resistance against cancer dissemination.

4. The earlier the primary growth is eliminated, the less likelihood of demonstrable lymph node involvement.

5. Even if a limited number of these do become grossly involved, the disease might still be controllable.

It is unfortunate that inferential, if not plain spoken, doubt as to the possibility of controlling demonstrably cancerous nodes by proper surgical removal frequently emanates from accepted "authorities" based chiefly upon their own lack of personal experience or lack of observation of the work of men accustomed to do this kind of surgery. That a worth-while percentage of these cases can be salvaged, even those with palpable nodes, is proved by the experience of many surgeons of unquestioned standing who have followed the teachings of Butlin, Roux, Crile, Kocher, etc., the combined published statistics from all these being of sufficient volume and detail to be irrefutable.*

Many radiotherapists have criticized mass cervical node excision, prophylactic or therapeutic, on the ground of its supposedly high essential mortality, citing in proof of this statistics of operations done

*In a series of 70 of our own cases treated before October, 1928, that were so far advanced as to require the combined operation of removing lymph nodes and primary growth at the same sitting, there were 16 cures of from five to eighteen years (22.86 per cent). In 29 of the 70 cases the glands were apparently negative, with cures of 20.6 per cent; while in 41 cases the glands were definitely positive, with cures of 24.5 per cent. For the whole series there were 23 per cent cures and a 34 per cent post-operative death rate. Our average of five-year-plus cures for the two-step operation for the same previous-to-1930 period was 46 per cent with a 5 per cent postoperative death rate. (See Blair and Brown.)

For the subsequent series cared for before 1932, we had 11 mouth cancers with complete operation in one step, with 36.6 per cent living five or more years and 11 cases operated upon in two stages with 55 per cent living five or more years. In this second series there were no postoperative deaths for the two-step operation and 18 per cent for the one-step operation. The lessened operative mortality of the latter series was due to almost no radical change in the operative procedure and to improvement of the organization of our house service and to the elimination of a group of five years later. Of those in the earlier group having a complete one-step operation, 1 out of each 5 died before complete postoperative recovery and a 33 per cent chance for a five-year-plus cure, while of those in the later group 1 out of each 11 died post-operatively and 49 per cent plus had five-year-plus cures. (See Blair, Brown, and Byars.)

have seen many cases in which, from the history and the description of the mouth lesion, we felt a positive diagnosis should have been made without hesitation on the clinical picture alone, but which had been allowed to become far advanced or inoperable because of that rather stereotyped laboratory return of "no cancer found" (Fig. 6). The finding of pus in a suspected neck does not of itself eliminate the possibility of cancer being present.

The majority of incurable lip cancers which we have observed were such because of cervical metastases rather than from spread by continuity, and in some of these the primary lesion had already been completely controlled.



Fig. 6.—Illustrating ingrowing types of epitheliomas. *History:* Patient aged 65 years. He had a sore on lip for eighteen months which had received a great deal of radiation. *Findings:* Induration of practically the whole lower lip with a nodular fissure; loss of beard and glazed skin from radiation; hard nodes in both sides of neck. *Treatment:* Block excision of entire lower and part of upper lip, suturing mucosa to skin. Complete right-sided neck dissection. Dissection of left side postponed because the removed glands were reported negative. *Microscopic examination* of lip showed squamous-cell carcinoma. Right nodes were reported microscopically negative, and the patient did not return for the left-side neck dissection. We were informed by letter that the patient died one year later, and that "the neck lumps had come through the skin and caused hemorrhage." The pathologist had failed to identify cancer in the nodes of the right side, but the clinical picture and subsequent outcome were both typical of cervical node metastasis.

RECAPITULATION

Too often in the recent past more attention has been focused on simplified treatment of the primary lesion than upon the cure of the patient. The greatest assurance of both, in the simplest fashion, can be accomplished by:

1. Early removal and microscopic examination of all possibly pre-cancerous lesions or a cautery-biopsy examination of the more advanced. The first will prevent many cancers; the latter will be of great help in planning treatment of the case in hand.

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For the subsequent series cared for before 1932, we had 11 mouth cancers with complete operation in one step, with 36.6 per cent living five or more years and 11 cases operated upon in two stages with 55 per cent living five or more years. In this second series there were no postoperative deaths for the two-step operation and 18 per cent for the one-step operation. The lessened operative mortality of the latter series was due to almost no radical change in the operative procedure and to improvement of the organization of our house service and to the elimination of a group of five years later. Of those in the earlier group having a complete one-step operation, 1 out of each 5 died before complete postoperative recovery and a 33 per cent chance operatively and 49 per cent plus had five-year-plus cures. (See Blair, Brown, and Byars.²)

for control of true mouth cancers which in different operative series of our own cases, as cited above, has varied from 0 to 45 per cent, depending chiefly upon the stage of advancement of the cases. Large or small, however, this death rate has no real bearing on that to be expected from neck dissections done for early lip cancers. As previously stated, we see too few of the latter to present real statistical value, but, based on some observation of the latter cases, we feel that prophylactic upper neck dissection for early cases should be about as free from mortality as any major operation in surgery. That there might be an essential mortality percentage following complete neck dissections done for advanced gland involvement from a high grade lip cancer is a self-evident fact, but untreated the death rate of such cases is just about 100 per cent; until radiotherapy can present satisfactory statistical evidence of a reasonable percentage of five-year-plus control for these advanced cases, even a 10 per cent mortality from well-planned surgical attempts would be open to criticism, chiefly because every operative death tends to prevent future sufferers from seeking indicated surgery at a stage of the disease when surgery would have a fair chance of being both helpful and free from danger. Quick voices the sentiments of Edwards,² Martin, and many other radiologists when he states that because "a healthy lymph node can digest and destroy tumor emboli . . . therefore the lymph nodes should not be excised." But how are we to be sure that the lymph nodes in the particular case still remained healthy?

Though it is generally accepted that lymphatic metastasis results from the passage of some sort of cancer material from a primary lesion through a lymph channel to lodge in a node, (a) how and (b) when is node contamination hastened or retarded and (c) what factors hasten or retard it, and what initiates the change from dormant contamination to actual demonstrable metastatic growth within the node? The answers to these questions all still remain matters for interesting, if not profitable, speculation. From neither the clinical characteristics nor the microscopic picture can we make more than a guess as to how early or how late the individual primary lip, mouth, or face cancer will cause cervical gland metastasis or whether or not it will ever occur.

1. We assume that cancer material or a cancer cell breaking free from the parent growth is carried to the gland through a lymph channel, but few, if any, microscopists have ever actually recognized either the exfoliation, the passage of the cancer material through the lymph vessel, or the early characteristics of the cancer material that has already found lodgment within a node (Fig. 6); and, unless we can grant to either the lymphatic vessels or the newly divided neck tissues a faculty of destroying cancer, the second and third of our previously cited "accepted facts" are both apparently somewhat unreconcilable with Butler's successful practice of removing the glands en masse ten days or two weeks before performing the tongue amputation.⁴

2. As already cited, we apparently can have no knowledge of the exact time of gland contamination.

3. It is a modern teaching that a moderate amount of radiation to the gland area may prevent or delay the development of metastases, but as far as we know this is not proved and certain of our own experiences have suggested the possibility that partial irradiation of the nodes incidental to the treatment of the primary growth might on the contrary stimulate the metastatic growth; we have modified some of our technical procedures to anticipate this possibility. Certain clinical observations suggest that trauma can hasten the glandular metastasis, and we have seen several such instances.

It is well known that certain epitheliomas of more or less distinct clinical characteristics and of somewhat corresponding histology are more apt to, and on the average will more quickly, cause gland metastasis than will certain others, and this fact is with propriety often taken into consideration in making a tentative estimate of the likelihood of present or future gland metastases in the individual case. However, in making this estimate, as a rule, most have failed to credit the gland function with any active power to kill cancer cells, apparently regarding the latter as a sort of static, somewhat like that of the trap under the pantry sink. However, there are several clinical observations bespeaking the contrary. One is the dormant period already cited. Another is the long periods of time that an active metastasis can develop and increase in one node without demonstrable invasion of any neighbor, while less frequently a whole mass of related glands will enlarge almost simultaneously, this latter sometimes following an injury. Another example of special resistance is the great rarity with which epithelial cancer arising in the face or mouth ever will metastasize below the clavicle. With the exception of an occasional axillary node enlargement, in all but two of the few cases we have seen of generalized metastases from face or mouth, the first recognized symptoms have been of liver involvement, ascites, etc. The mechanism or chemistry which sustains this special protection might not differ in essence from that guarding our whole organism, but it has a special significance with supraclavicular cancer, for in the vast majority of cases total elimination of the latter would amount to a cure, free from the danger of distant recurrence.

This behavior of the nodes might suggest the presence of some material that gives to the gland an active but variable resistance against the development of cancer emboli.

Be this as it may, until the above or some other type of biologic control is given us, our present function still remains the early recognition and destruction of the primary lesion with due regard for possible or probable present or future metastases. It stands to reason that the more acceptable the remedy, the earlier will be the average time of treatment, but acceptability should not be allowed to compromise

efficiency. Radiation is the most generally acceptable, and when properly done it has a high average of efficiency in controlling the primary lip lesion, but we have not found this true in regard to the lymph nodes.

That the average treatment does not truly reflect the potential efficiency of present-day medicine for the control of this disease is suggested by the fact that we still see a rather small percentage of early lip, face, and mouth cancers, most of them having previously been observed or subjected to some essentially inadequate plan of treatment.



Fig. 7.—Illustrating a large, rapidly "outgrowing," cauliflower mass, clinically of low malignancy. *History:* Patient aged 75 years. He had a wart on left lower lip for many years and three years previous to our examination had consulted a physician who gave him "treatments" and applied paste. The lesion continued to increase in size and became dry and cracked. *Findings:* A large cauliflower mass, shown in illustration was present, but without ulceration and no node involvement mentioned. *Treatment:* Destruction with soldering iron cautery was performed and a repair was made from forehead flaps. The neck was not opened. *Result:* Six years later, at the age of 81 years, he had a severe fall, with fractured ribs. The patient was in poor condition, but without sign of recurrence. He died shortly after this. *Microscopic examination:* Squamous-cell carcinoma.

In some, if not the majority of, instances this has not been due entirely to the victim's own negligence. The past and present concentrated efforts of certain in our profession plus those of the public health, social, and educational agencies to make the public cancer-conscious have not been wasted as far as the laity is concerned. Nor can the physician

previously consulted be justly held entirely responsible for faulty advice or the inadequate treatment given. Lip and mouth cancers are not of common occurrence and the average practitioner is seldom a special student of these lesions; therefore he must look to higher "authority" for guidance. When he finds the accredited teachers apparently divided in their expressions, it is but natural that he should attempt to carry out his own interpretation of what he takes to be the simplest plan presented, but possibly without any real understanding of what was meant or what is needed for its execution.

It is comparatively simple to state underlying principles of any plan of cancer treatment, but, owing to the varying conditions that must be met in actual practice, their successful application will depend as much



Fig. 8.—Illustrating the "ingrowing" type of epithelioma. *History:* Patient aged 26 years. He has had a central lip fissure for a year which is now enlarging laterally. *Findings:* Patient had a small "scooped-out" ulcer with slight induration. *Treatment:* Biopsy of lip ulcer was performed, followed by radium and later upper-neck gland excision of both sides. *Microscopic examinations* of lip and glands both showed squamous-cell carcinoma.

upon the subeonscious judgment that comes from long intelligent observation as upon any rule-of-thumb. Somehow one gets the impression that certain writers, in their efforts to simplify and at the same time broaden the scope of the latter, have occasionally tricked themselves into advocating practices they would not, or should not, always follow. We should never lose sight of the accepted principles upon which our plan of treatment is based, nor the fact that each individual lip cancer is an individual problem. The plan for its proper treatment may be influenced or modified by any number of factors: the age and condition of the patient, the kind and number of previous treatments, the duration of the lesion, the rate of growth or a change in rate, the presence,

absence, or character of node enlargement, and the physical characteristics of the primary lesion; these and others all must be considered. For instance, it is an old and long-accepted observation, which can now be classed as knowledge, that the mere size of the primary lesion means little, but the direction in which it grows is of the greatest significance. When the latter is outward, away from the surface, intensity of its virulence may be in inverse ratio to its size (Fig. 7) but with growths and ulcerations that invade the underlying tissues (Fig. 8) the seriousness of the case is apt to be in indirect proportion to the size and depth of the invasion. Some very minute or undiscovered ulcers can cause widespread gland involvement, while other huge masses may show no cancer in the related lymphatics.

Microscopic grading does give positive evidence of malignancy to the extent of its positive findings, but does not exclude the presence of an unrevealed area of a higher grade than that actually observed. On the other hand, the microscopic lip picture should be rated maybe as much as two degrees less virulent than the same picture found in a tongue lesion, but there is no warrant for ever permitting high microscopic grading alone to deprive the patient of the chance of control that might come from wide excision or a well-performed neck dissection. Can the general practitioner who usually first sees these cases be expected to compass all of the above and more from a few trite rules based often upon a large series of cases but possibly questionable follow-ups and which he may find contradicted in the next article he reads on the subject?

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ARTERIOSCLEROSIS IN PANCREATIC DIABETES*†

LESTER R. DRAGSTEDT, M.D., DWIGHT E. CLARK, M.D.,
ORMAND C. JULIAN, M.D., C. VERMEULEN, M.D.,
AND W. CARTER GOODPASTURE, M.D.,
CHICAGO, ILL.

(From the Department of Surgery of the University of Chicago)

THE extensive literature on arteriosclerosis has been recently collected in a book¹ published under the auspices of the Josiah Macy, Jr., Foundation, and will not be reviewed here. A consideration of this literature indicates that, whereas much significant information has been obtained, the pathogenesis of this disease remains obscure. As pointed out by Wells² the fact seems undeniable that the arterial colloids, like those elsewhere in living tissue, undergo definite changes with age, leading to their progressive dehydration and loss of elasticity, and that these changes in the arterial walls in time must result in gradual dilatation and elongation of the vessel. However, the development of atheromatous lesions in the intimal layers with calcification does not take place in the arteries of all old people and there is some basis for the view that some of these changes are not inevitable but may be due to some metabolic defect. The experimental production of atherosclerosis in the aortae of rabbits by the feeding of cholesterol, as in the experiments of Anitschkow,³ Leary,⁴ and others, furnishes strong support for this view. Leary has presented convincing evidence with respect to the similarity between these experimental lesions and atherosclerosis in man.

The abnormally high incidence of presenile arteriosclerosis in diabetes mellitus has been generally recognized. Joslin⁵ and his associates in particular have called attention to this complication and it has recently been commented upon by a number of observers (Morrison and Bogan, 1929,⁶ Rabinowitch, 1935,⁷ Hallock, 1936,⁸ Ruprecht, 1938,⁹ and Root and associates, 1939.¹⁰ The defect has not been abolished by insulin therapy and constitutes one of the chief disabling complications of diabetes today. There seem to be no essential differences between the blood vessel changes that occur in diabetes and those that develop in old age and are often attributed to senility. It is the purpose of this paper to record the occurrence of arteriosclerosis in depancreatized dogs in greater incidence than that commonly found in this species.

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According to Fox,¹¹ the domestic dog rarely exhibits arteriosclerosis. After the fifth year hyperplasia of the intima may occur, but the deposition of calcium is very rare. In the wild relatives of the dog arteriosclerosis was found in 3 of 192 specimens of material in a zoo. The life span of these animals was one-third longer than the average for their family.

In 1924 Fisher¹² observed very marked arteriosclerosis of the aorta in a partially depancreatized dog that had survived the operation for eight months.

EXPERIMENTAL OBSERVATIONS

1. *The Incidence of Arteriosclerosis in Depancreatized Dogs.*—The material upon which this report is based consists of mongrel dogs of both sexes obtained from the city pound and subjected to partial or complete pancreatectomy. During the past five years, we have had under observation approximately 225 depancreatized animals in which the diabetes was fairly accurately controlled with both regular and protamine zinc insulin. For the most part these animals were used in the investigation which resulted in the demonstration of a second internal secretion of the pancreas, apart from insulin, and which has been designated lipocaine as having to do with the utilization of fat. Reports of this work have appeared elsewhere.¹³

During the course of routine autopsies in connection with this study, we have found varying degrees of arteriosclerosis of the aorta in 10 completely depancreatized and in 1 partially depancreatized animal. In the earlier part of the work sufficient attention was not paid to the possibility of alterations in the blood vessels and careful examinations of this region were not made. The 11 instances in which changes were found occurred in the last 80 animals coming to autopsy, which would indicate an incidence of about 13 per cent. The lesions have been observed most frequently as small raised pale yellow or white nodules in the intima of the thoracic and abdominal aorta, arranged in clusters about the orifices of the intercostal, mesenteric, and renal arteries and in the first part of the aorta near the base of the aortic valves (Figs. 1 and 2). Microscopically, all degrees of involvement have been found, from proliferation and thickening of the intima, deposition of amorphous lipid material in the subintimal layers, and disruption of the media with deposition of amorphous lipid and calcareous material (Figs. 3-7). These changes have been found commonly in dogs from five to nine months after pancreatectomy, but lesions of lesser extent have been observed as early as five weeks after the operation. The observation of typical atheromatous areas in the aorta of a depancreatized dog only six months old (Fig. 8) that was raised in the laboratory is especially interesting since it indicates that this complication can occur in very young animals. Abbreviated protocols of two of the animals follow.

PROTOCOLS

Dog 665.—Male, mongrel, aged about 1 year. Pancreatectomy on Aug. 24, 1937. Diet: bread, meat, and milk, containing approximately 25 per cent fat. Diabetes controlled with protamine insulin, 4 units daily. By Sept. 24, 1937, liver became very fatty (40 per cent fat). Lipocaine given from Nov. 11, 1937, to Feb. 26,

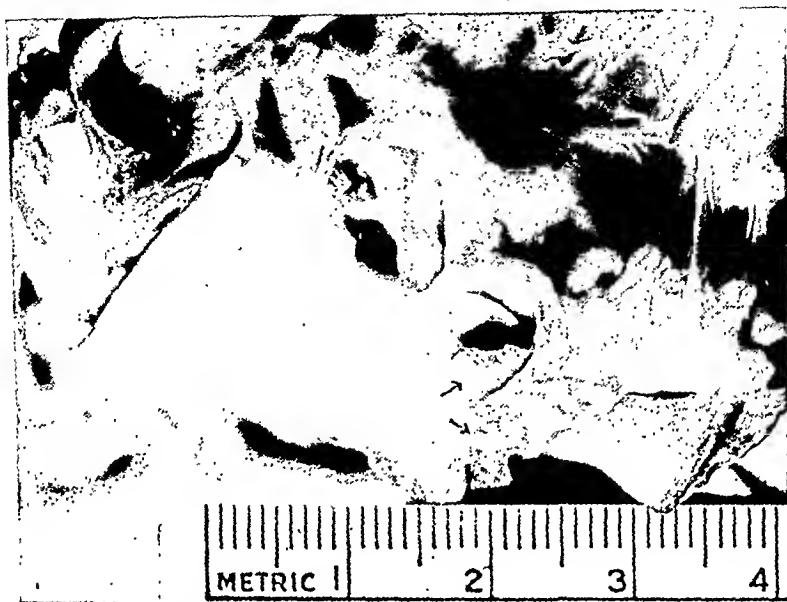


Fig. 1.—Dog 665. Photograph showing arteriosclerosis at the base of the aortic valves and about the orifices of the coronary arteries in a dog nine months after pancreatectomy.



Fig. 2.—Dog 665. Photograph showing numerous raised yellow nodules in the intima of the thoracic and abdominal aorta at the orifices of the branching vessels in a dog nine months after pancreatectomy.

1938; clinical improvement and liver fat decreased to 8 per cent. Lipocaic stopped and animal became progressively weaker, lost weight, and died May 12, 1938.

Autopsy: Liver grossly normal; contained 6 per cent fat; no pancreas found; other organs, with exception of aorta, normal. When the aorta was opened, yellow-white nodules were seen and palpated on the intimal surface within the recesses of

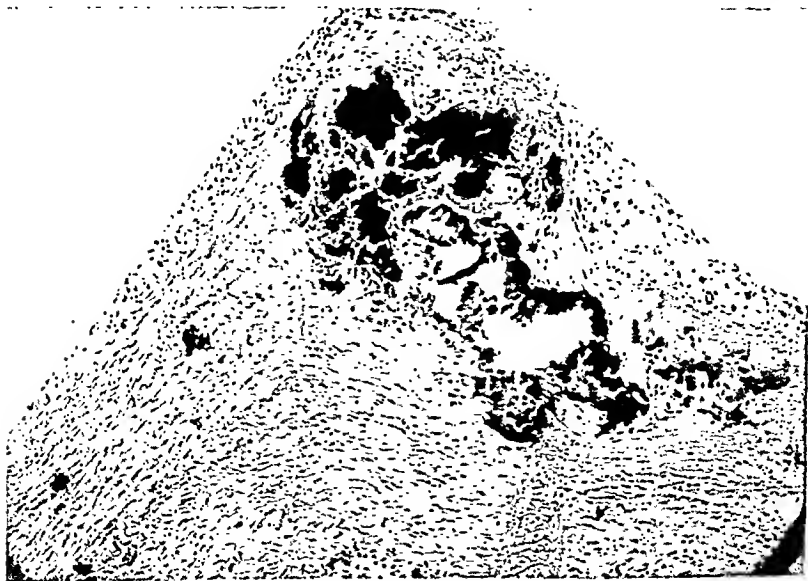


Fig. 3.—Dog 665. Photomicrograph showing details of lesions seen in Fig. 1. thickening of the intima, deposition of amorphous lipoid and calcareous material in the subintimal layers and in the media, and disruption of the fibers in the media.



Fig. 4.—Dog 665. Photomicrograph showing details of lesions shown in Fig. 2. Note intimal thickening and deposition of calcium and amorphous lipoid material in the media and in the layers beneath the intima.



Fig. 5.—Dog 241. This animal died five months after pancreatectomy and at autopsy nodules were found in the intima of the thoracic and abdominal aorta, as shown in Fig. 2. This section illustrates proliferation of intimal cells of the connective tissue type without disruption of the internal elastic lamina.



Fig. 6.—Dog 241. Photomicrograph showing thickening of the intima and deposition of calcareous and lipid amorphous material beneath the intima in a dog five months after pancreatectomy.

1938; clinical improvement and liver fat decreased to 8 per cent. Lipocaic stopped and animal became progressively weaker, lost weight, and died May 12, 1938.

Autopsy: Liver grossly normal; contained 6 per cent fat; no pancreas found; other organs, with exception of aorta, normal. When the aorta was opened, yellow-white nodules were seen and palpated on the intimal surface within the recesses of

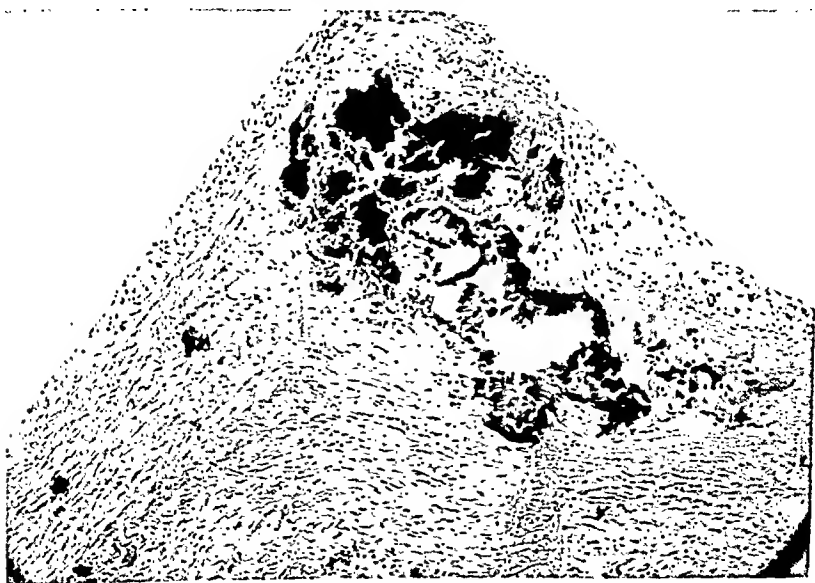


Fig. 3.—Dog 665. Photomicrograph showing details of lesions seen in Fig. 1, thickening of the intima, deposition of amorphous lipid and calcareous material in the subintimal layers and in the media, and disruption of the fibers in the media.

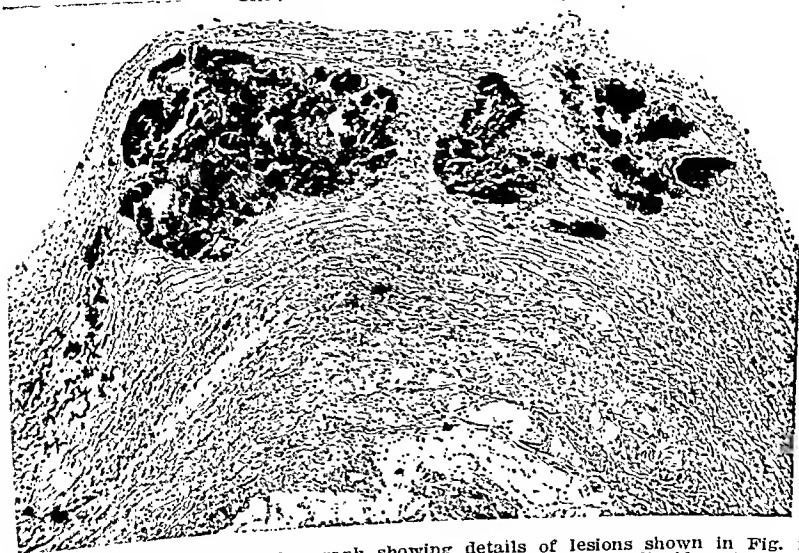


Fig. 4.—Dog 665. Photomicrograph showing details of lesions shown in Fig. 2. Note intimal thickening and deposition of calcium and amorphous lipid material in the media and in the layers beneath the intima.

2. *The Incidence of Arteriosclerosis in Normal or Nondiabetic Dogs.*—As indicated in the report by Fox referred to above, the occurrence of arteriosclerosis in normal domestic dogs has rarely been observed. However, during the past year we have examined the aortas of 75 normal or nondiabetic dogs, obtained from the same source, and somewhat to our surprise found definite arteriosclerosis lesions in 4, or about 5 per cent. These lesions were exceedingly small, consisting usually of one or two pale yellow or white nodules from 0.5 to 1 mm. in diameter and found usually in the first part of the aorta near the base of the aortic valves. Microscopic sections revealed essentially the same changes in the intima and media seen in the depancreatized animals.



Fig. 8.—Dog D-27. Photomicrograph showing arteriosclerosis of the aorta in a dog seven weeks after pancreatectomy. This animal was reared in the laboratory and was only seven months old at the time of death. A very marked fatty infiltration of the liver occurred and death resulted from the biopsy.

DISCUSSION

The finding of a higher incidence and great severity of arteriosclerosis in depancreatized dogs than in normal animals of this species presents another point of resemblance between pancreatic diabetes and diabetes mellitus as it occurs spontaneously in man. It seems probable then that factors found to be operative in the one case may be of significance in the other and that both in turn may throw some light on the pathogenesis of nondiabetic arteriosclerosis. Considerable evidence has accumulated incriminating certain factors in the development of presenile arteriosclerosis in diabetes mellitus and it is interesting that here, too, certain resemblances may be seen between the disease in man and in the experimental animal. While there has been some dissent, a number of writers (Joslin,⁵ Rabinowitch,⁷ and others) have voiced their

the aortic valves (Fig. 1) and the aortic ring felt calcified. Similar yellowish white raised nodules were observed in the intima near the ostia of the branches of the thoracic and abdominal aorta (Fig. 2). In the abdominal aorta, near the ostia of the celiac and renal arteries, could be seen faint white or yellow longitudinal streaking of the intima for a distance of 3 to 5 cm. Microscopic examination of these lesions (Figs. 3 and 4) revealed a marked hyperplasia of the intima, disruption of the media, and deposition of amorphous calcium and lipid material in the deeper intimal layers and in the media.



Fig. 7.—Dog 287. This animal died six months after pancreatectomy and at autopsy numerous small yellow nodules were found in the intima of the abdominal aorta and near the base of the aortic valves, as shown in Figs. 1 and 2. Section shows deposition of lipid and calcareous material in the media.

Dog 241.—Female, mongrel, aged about 2 years, weight 7.8 kg. Pancreatectomy on March 18, 1937. Diet same as for Dog 665. Diabetes controlled with protamine insulin, 8 to 14 units daily. On June 15, 1937, the liver was found to contain 32 per cent fat and the daily administration of lipocaic was started. On July 30, 1937, the liver fat was normal and lipocaic was discontinued. The animal then gradually lost weight and strength and died probably from an insulin convulsion on Aug. 14, 1937. Autopsy revealed a moderate fatty infiltration of the liver. No pancreas was found. The first portion of the aorta was normal, but numerous small pale yellow nodules (1 to 2 mm. in diameter) were seen in the intima of the thoracic and abdominal aorta near the ostia of the aortic branches. Microscopic examination revealed marked proliferation of the intima (Fig. 5) and in some deposition of amorphous lipid and calcareous material in the subintimal layers (Fig. 6).

of lipocaic to maintain normal fat metabolism as evidenced in some cases by repeated accumulations of fat in the liver and other findings indicative of lipocaic deficiency. The possible role of lipocaic deficiency in the presenile arteriosclerosis of diabetes mellitus and pancreatic diabetes is discussed.

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conviction that the incidence of arteriosclerosis in diabetes mellitus is especially high when diets rich in fat are employed and that conversely it has become more rare with the adoption of a low fat, high carbohydrate regimen. This suggests that some residual defect remains in diabetes mellitus even with adequate insulin therapy. Several years ago one of us (L. R. D.)¹⁴ raised the question: "Does this mean that many diabetics suffer from not only an insulin deficiency but also from a deficiency of lipocaic, which manifests itself in a disturbance in fat utilization, with the deposition of fat in the liver and in more chronic cases in the subendothelial layers of the arteries?"

There is some reason to believe that the atherosclerosis of the aorta in our depancreatized dogs may be due to lipocaic deficiency. Other investigators, with the exception of Fisher, have not observed this complication. Practically without exception these have followed the practice of Macleod and his associates¹⁵ of feeding fresh pancreas daily in addition to giving insulin. Fisher did not give fresh pancreas. The animals in our series that developed arteriosclerosis were maintained for varying periods of time on relatively insufficient amounts of lipocaic. For the most part they were used to assay the amounts of lipocaic in various pancreatic extracts and in this connection were allowed to develop the fatty livers of lipocaic deficiency alternating with periods of control.

Chaikoff and Kaplan,¹⁶ however, were able to keep depancreatized dogs alive for from one to five years by means of insulin but without providing raw pancreas or supplementary choline or betaine in the diet. These animals were not found to have arteriosclerosis. Examination of their paper reveals the interesting fact that these animals were provided a diet, adequate from the nutritive standpoint, but containing very small amounts of fat; i.e., only that present in raw lean beef. In a recent paper we^{13b} have reported the striking fact that the depancreatized dog on a low fat diet may survive for long periods on insulin alone; whereas, a high fat diet promptly produces the symptoms of lipocaic deficiency. In the series of animals reported here that developed arteriosclerosis, all were supplied diets containing from 25 to 45 per cent fat and active pancreatic juice was occasionally supplied to improve digestion and absorption.

SUMMARY

Arteriosclerosis of the aorta has been observed in 10 completely and 1 partially depancreatized dogs in our laboratory, representing an incidence of about 13 per cent where this complication was looked for. Lesions similar in nature but much less extensive were observed in 4 of 75 normal dogs of the same type and size and obtained from the same source, or an incidence of about 5 per cent. The depancreatized animals were well controlled with insulin and maintained on relatively high fat diets. Without exception these animals were given insufficient amounts

170). There was no edema, but the abdominal veins were very prominent and a loud continuous bruit could be heard over the lower abdomen. The posterior extremities were very weak. On Feb. 16 the animal was killed in a fight.

ANIMAL 5.—(Fig. 3.) An adult female collie; weight, 13 kg. An aorta-vena cava fistula was established on Dec. 17, 1938; aorta, 7 mm. in diameter; vena cava, 9 mm. in diameter; fistula, 5.5 mm. long. A roentgenogram was taken before opening the fistula (pulse, 132). Five hours after opening the fistula a marked diminution in cardiac size had occurred (pulse, 160). On Jan. 3, a slight cardiac dilatation

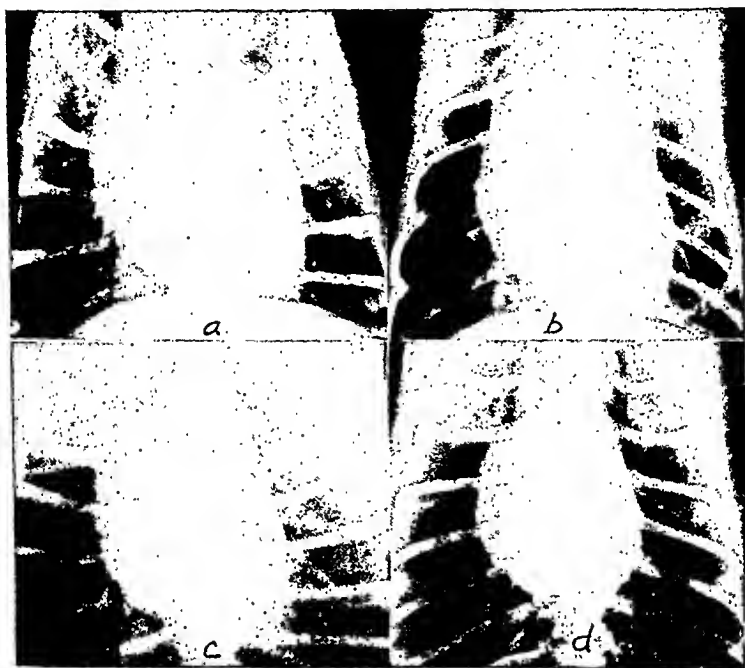


Fig. 1.—Animal 8. Roentgenograms of heart following establishment of an aorta-vena cava fistula. *a*, 10:45 A.M., just before opening fistula; *b*, 11:15 A.M., fifteen minutes after opening fistula; *c*, 1:30 P.M.; *d*, 4:00 P.M. At 6 P.M. the animal died as the result of the fistula.



Fig. 2.—Animal 4. Roentgenograms illustrating reduction in size of heart four hours after opening an aorta-vena cava fistula. The animal died a few hours later, *a*, Normal heart; *b*, four hours after operation.

THE ANATOMIC AND PHYSIOLOGIC EFFECTS OF AN ARTERIOVENOUS FISTULA*

EMILE HOLMAN, M.D., SAN FRANCISCO, CALIF.

(From the Laboratory for Surgical Research, Stanford University School
of Medicine)

SIGNIFICANCE OF DIMINUTION IN CARDIAC SIZE ON OPENING A FISTULA

THAT an arteriovenous fistula has profound effects upon the circulatory system is universally recognized, although the explanation for some of these effects is still subject to controversy. Particularly puzzling has been the effect upon the size of the heart, which is said invariably to become enlarged in consequence of the fistula. This enlargement has been attributed by some solely to dilatation,¹ but by others to a high degree of hypertrophy.² A startling fact, however, is the observation, repeatedly made, that in the first twenty-four hours after the establishment of an experimental arteriovenous fistula, the heart diminishes in size, followed in succeeding days by a gradual enlargement of the heart. Inasmuch as this sequence of events has recently been questioned,³ the following observations are presented:

ANIMAL 8.—(Fig. 1.) Female adult dog; weight, 9 kg. An aorta-vena cava fistula was established on Jan. 24, 1939; aorta, 6.5 mm. in diameter; vena cava, 8.5 mm. in diameter; fistula, 5.5 mm. long. Before opening the fistula (10:45 A.M.), a roentgenogram of the chest was taken (pulse, 120). At 11:15 A.M. a second roentgenogram showed a slight diminution in cardiac size (pulse, 120). At 1:30 P.M. the cardiac size was even smaller (pulse, 132), and at 4:00 P.M. the heart was remarkably smaller (pulse, 200). At this time there was marked edema of both lower extremities. The animal died at 6:00 o'clock, two hours later.

ANIMAL 4.—(Fig. 2.) Adult male; weight, 12 kg. An aorta-vena cava fistula was established on Dec. 21, 1938; aorta, 7 mm. in diameter; vena cava, 10 mm. in diameter; fistula, 7 mm. long. Before opening the fistula a roentgenogram of the chest was made (pulse, 88). All clamps (proximal artery, distal artery, distal vein) were removed except the clamp on the vein proximal to the fistula. No bruit or thrill developed and the pulse increased only to 104. After releasing the clamp on the proximal vein, a loud bruit was heard immediately and an intense thrill could be felt. The pulse now increased to 140. A roentgenogram four hours after operation showed a remarkably small heart (pulse, 160). The next morning the animal was found dead.

ANIMAL 7.—Male pup; weight, 6.8 kg. An aorta-vena cava fistula was established Jan. 10, 1939; aorta, 5.5 mm. in diameter; vena cava, 8 mm.; fistula, 4 mm. long. Before opening the fistula a roentgenogram of the chest was made (pulse, 120). One hour after opening the fistula, a definite decrease in the size of the heart was noted (pulse, 132). Two days later there was still a slight reduction in the size of the heart. On Jan. 17 a definite increase in the cardiac shadow had occurred (pulse,

*This study was aided by a grant from the Fluid Research Fund of the Rockefeller Foundation.

thetia, an adult dog was given 0.5 c.c. of histamine (1:1,000) causing a marked fall in blood pressure from 144 mm. to 66 mm. Hg (Figs. 4, 1 and 2). Coincident with this fall in blood pressure there occurred a marked reduction in cardiac size (Figs. 4, 1' and 2'). Histamine shock is produced by peripheral vasodilatation. This results in a redistribution of the circulating blood volume, decreasing it in the central circulatory bed and increasing it in the peripheral bed. As a direct consequence of this redistribution of blood volume, the heart is reduced in size. In the same experiment the animal was permitted to recover both its blood pressure and its normal cardiac size (Fig. 4). Again,

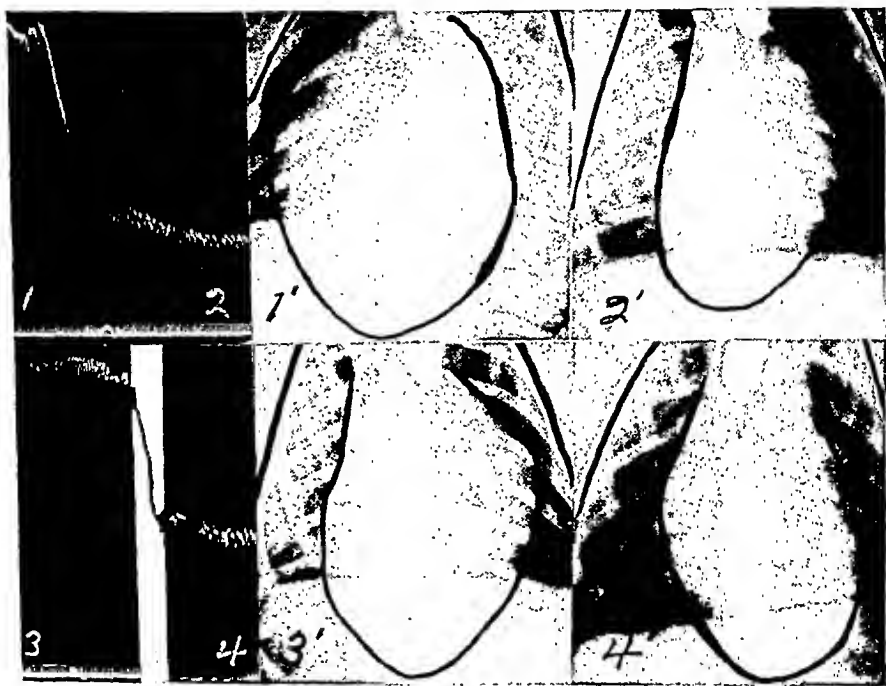


Fig. 4.—Shock and cardiac size. The kymographic record (1 and 2) illustrates the fall in blood pressure produced by an injection of 0.5 c.c. histamine. Coincident with this histamine shock the heart decreased in size as shown in roentgenograms 1' and 2'. Following recovery of blood pressure (3) and cardiac size (3'), shock (4) was produced again by trauma upon the thigh, accompanied again by a decrease in cardiac size (4').

shock was precipitated by heavy and repeated blows on one thigh. The mechanism underlying this shock is undoubtedly related to the loss of blood into the traumatized area.^{4, 5} The development of shock and drop in blood pressure (Fig. 4, 3) was accompanied by a corresponding reduction in cardiac size (Fig. 4, 3'). Again this is explicable on a redistribution of the total blood volume, the blood lost into the peripheral tissues being abstracted from the central circulatory bed.

Exactly comparable observations have been made incident to severe blood letting. A progressive diminution in cardiac size accom-

was noted (pulse, 180), and on Feb. 21 a marked dilatation was present (pulse, 156). At this time it was also noted that the abdominal wound was discharging pus, and, although a loud bruit was then present, from this time forward the bruit gradually diminished and finally disappeared entirely. Necropsy (Aug. 17, 1939) showed closure of fistula by thrombosis and fibrous contraction.

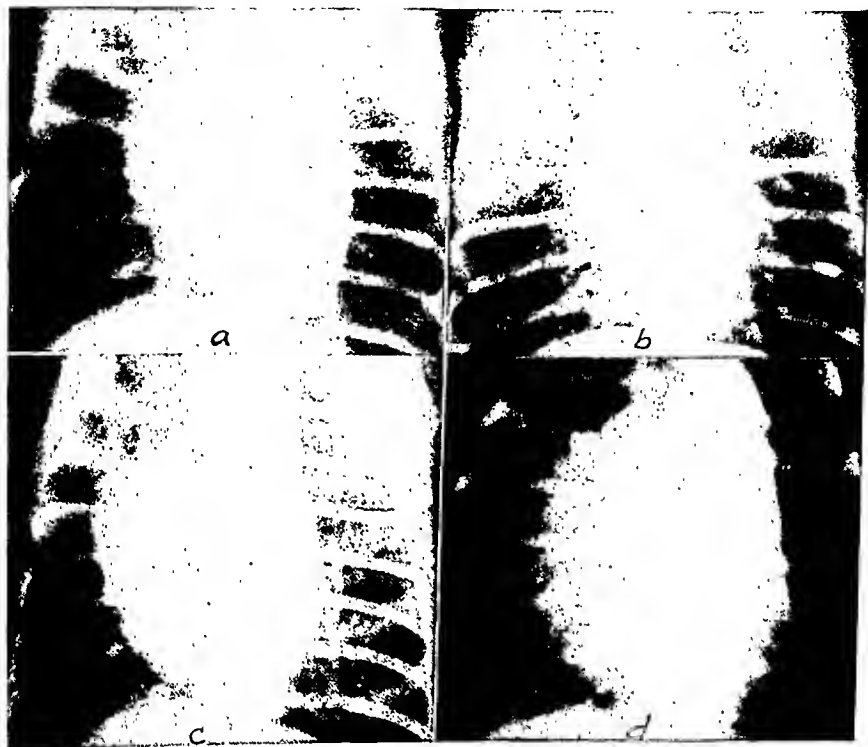


Fig. 3.—Animal 5. Roentgenograms illustrating diminution in cardiac shadow within four hours after establishing an aorta-vena cava fistula, a definite, though slight, dilatation five days later, and a marked dilatation seven weeks later.

ANIMAL 3.—Adult male; weight, 15 kg. On June 30, 1938, a fistula between the right femoral vessels was established: artery, 4.5 mm. in diameter; vein, 6 mm. in diameter; fistula, 2.4 cm. long. A roentgenogram was made before opening the fistula (pulse, 104). Immediately after opening the fistula the pulse rate increased to 130. At the same operation, a fistula between the left femoral vessels was established: artery, 4.5 mm. in diameter; vein, 6 mm. in diameter; fistula, 2.7 cm. long. Before opening this second fistula the pulse rate was 144. After opening the second fistula the pulse rate rose to 160. Six hours later a roentgenogram showed a definite diminution in cardiac size. Both lower extremities were considerably swollen and edematous. Within six days this edema subsided, but the superficial veins became prominent. Within five days the heart recovered its normal size (pulse, 160), and a month later it was considerably larger than normal (pulse, 156). The animal is still living.

These variations in cardiac size incident to an arteriovenous fistula are directly comparable with the reduction in the size of the heart accompanying shock. In an acute experiment, under nembutal anes-

establishing an aorta-vena cava fistula, the animal invariably died if the lateral anastomosis produced between the two vessels equaled in length the diameter of the aorta. In such instances, the diversion of blood into the venous bed was excessive, the blood pressure in the cerebral, coronary, and renal arteries was reduced to a minimum, the heart diminished markedly in size, and death followed.

In establishing a femoral fistula, the lateral anastomosis between the vessels can be 2 and 3 cm. in length, since the volume of blood diverted into the venous bed is limited by the diameter of the proximal artery. As the proximal artery dilates, the long lateral anastomosis permits an increasing leakage of blood into the venous bed, and the usual physiologic and anatomic effects invariably will occur. Experience has taught us that, unless the small femoral vessels are joined through long lateral anastomoses, the opening will close by thrombosis and cicatricial contraction. Small openings cause so little diversion of blood that no measurable physiologic or anatomic changes will occur; i.e., measurable by present instruments of precision. End-to-end anastomoses have usually proved to be quite ineffective in producing these physiologic results, since complete division of the artery is followed by an elastic contraction both in length and in transverse diameter of the vessel, so that the fistula is, and remains, too small for an effective diversion of blood.

When fistulas compatible with life but still capable of diverting a large volume of blood are established, the reduction in size of the heart is invariably followed by a gradual dilatation of the heart, in some instances of remarkable degree, as the following experiments demonstrated.

INCREASED CAPACITY OF CIRCULATORY SYSTEM DUE TO CARDIAC DILATATION
AND DILATATION OF ARTERY AND VEIN BETWEEN THE FISTULA AND
HEART, WITH A CONCOMITANT INCREASE IN TOTAL BLOOD VOLUME

To determine more exactly the effects of an arteriovenous fistula, the following experiments were undertaken in the growing animal. Three puppies from the same litter, born July 6, 1938, all approximately equal in size and weight, were chosen for the experiment, one being kept as a control.

PUP 1.—Male; weight, 9 kg. On Nov. 29, 1938, an aorta-vena cava fistula was established: aorta, 6 mm. in diameter; vena cava, 8 mm. in diameter; fistula, 5 mm. long. The pulse rate was immediately accelerated from 120 to 172 on opening the fistula. According to roentgenograms, a slight diminution in the cardiac shadow occurred immediately after the opening of the fistula, but within twenty-four hours the heart had recovered its original size, followed in the succeeding months by a truly enormous enlargement of the heart. At all times after the establishment of the fistula, good femoral pulsations were present on both sides. On April 24, 1939, the pulse rate was 192; respirations, 52; the heart was very much enlarged and there was great dyspnea on exertion. On Nov. 7, 1939, the animal was in much better condition; there were no edema and no ascites;

panied massive external hemorrhage (Fig. 5), followed by recovery of the heart to normal size as the withdrawn blood was restored to the circulatory system.

The opening of an arteriovenous fistula also causes bleeding, but in these circumstances the bleeding does not occur to the outside nor into the tissues, but into a capacious venous system distal and proximal to the fistula, capable of storing in it a large volume of blood. This redistribution of blood from the central circulatory bed into the peripheral venous bed is accompanied inevitably by a reduction in the size of the heart, provided the fistula permits a sufficient diversion

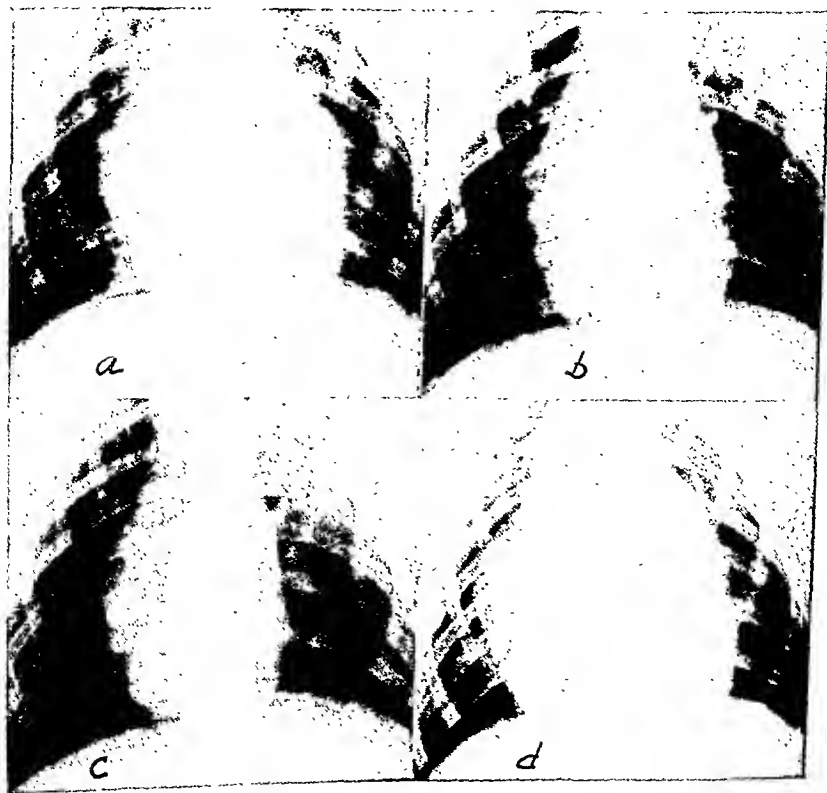


Fig. 5.—Roentgenograms illustrating the direct relationship between size of heart and total volume of circulating blood. *a*, Normal heart of 12 kg. dog; *b*, after removal of 200 c.c. blood from femoral artery; *c*, after removal of additional 300 c.c. blood; *d*, after restoration of 400 c.c. blood into femoral vein. The size of heart is even larger than the normal heart due to accretion of fluid from tissues into the circulatory bed during the bleeding process.

of blood from the arterial bed. The diminution of the cardiac size in these instances was quite independent of the rate of cardiac contraction, since subsequent dilatation was often accompanied by a pulse rate equal to or higher than the rate when the heart was diminished in size.

Such effects upon the heart are dependent upon two conditions; namely, the size of the fistula and its location in the arterial tree. In

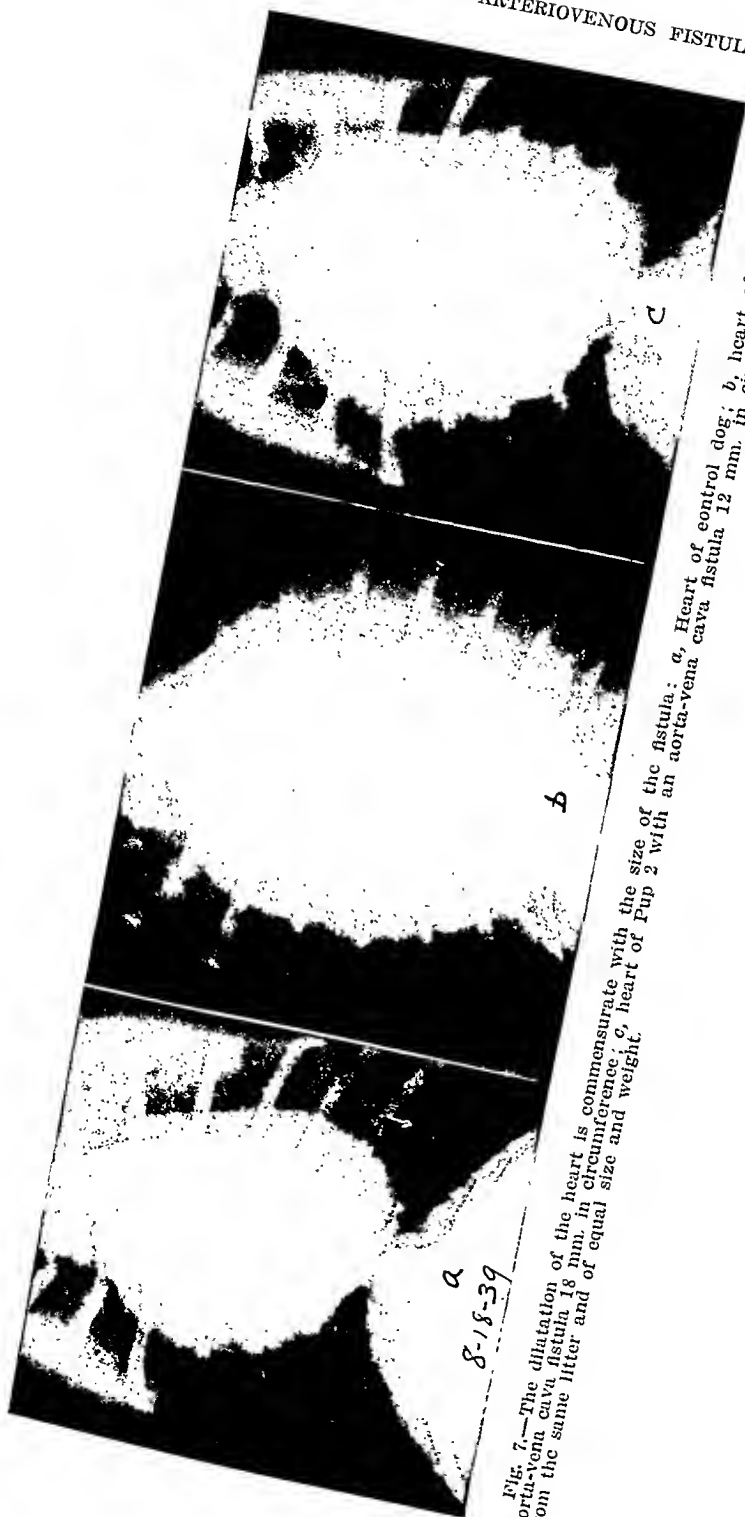


FIG. 7.—The dilatation of the heart is commensurate with the size of the fistula: *a*, Heart of control dog; *b*, heart of Pup 1 with an aorta-vena cava fistula 18 mm. in circumference; *c*, heart of Pup 2 with an aorta-vena cava fistula 12 mm. in circumference. All animals from the same litter and of equal size and weight.

good femoral pulsations were palpable, large veins (Fig. 11) were visible over the abdominal wall, and a loud bruit was audible over the lower abdomen. On this date, approximately one year after the establishment of the fistula, the carotid artery was cannulized to obtain a continuous record of the blood pressure. The fistula was exposed and closed by compression. Immediately there occurred a pronounced increase in blood pressure and a fall in pulse rate (Fig. 6). Analyzing this kymographic record, we find that closure of the fistula increased the mean systolic pressure from 186 to 236 mm. Hg immediately after closing the fistula, dropping to a level of 212 mm. Hg as long as the fistula remained closed, falling precipitately on opening the fistula to 140 mm. Hg, but recovering promptly within a few beats to the previous level of 186 mm. Hg. Variations in pulse rate paralleled these changes in blood pressure. The animal was killed, and examination revealed an aorta dilated from the heart to the fistula and a greatly dilated vena cava from the fistula to the heart. The heart almost filled the chest. The fistula admitted a bougie having a circumference of 18 mm. The circulatory system was injected with bismuth oxychloride in gum acacia (Fig. 8). The heart weighed 176 gm.; weight of animal, 11.1 kg. (Fig. 9).

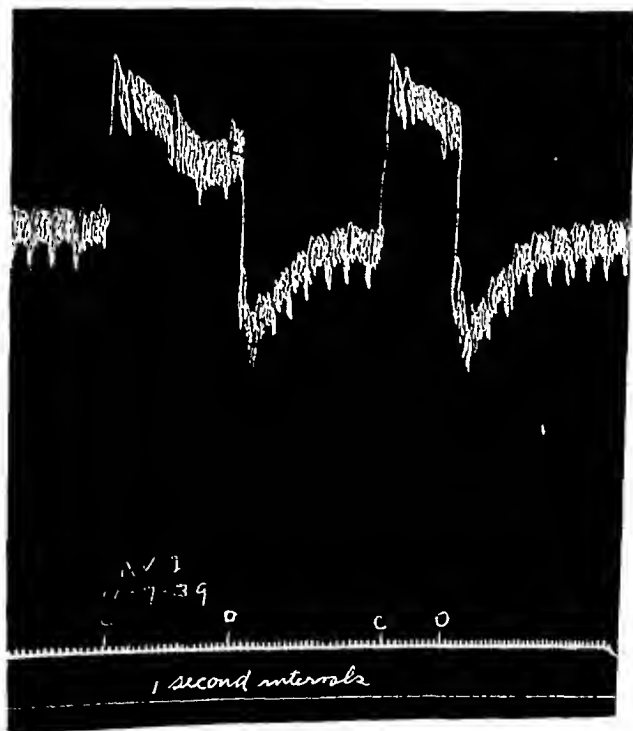


Fig. 6.—Pup 1. Marked elevation of blood pressure and reduction in pulse rate on closing an aorta-vena cava fistula of eleven months' duration.

PUP 3.—Male; weight, 8.3 kg. On Dec. 6, 1938, an aorta-vena cava fistula was established: aorta, 5 mm. in diameter; vena cava, 8 mm. in diameter. On opening the fistula the pulse rate rose from 132 to 160. On the following day a good pulse could be palpated in both femoral arteries, there was no edema, and the pulse rate was 180. A roentgenogram taken twenty-four hours after establishing the fistula showed a definite decrease in the size of the heart. On Dec. 8, 1938, the heart had

The animal was killed and the circulatory system injected with bismuth oxychloride in gum acacia. The aorta and vena cava were both dilated from the fistula to the heart (Fig. 8) and the heart was greatly enlarged. The heart weighed 123 gm.; weight of animal, 10 kg. (Fig. 9). From the lesser cardiac enlargement as compared with Pup 1, it was considered probable that the fistula was smaller in this animal than in Pup 1. This proved to be the case. The fistula admitted a bougie having a circumference of 12 mm., as compared with 18 mm. in Pup 1.

The control animal was also killed on this date, and the heart and circulatory system injected with bismuth oxychloride (Fig. 8). The heart weighed 74 Gm.; weight of the animal, 11.6 kg. (Fig. 9).

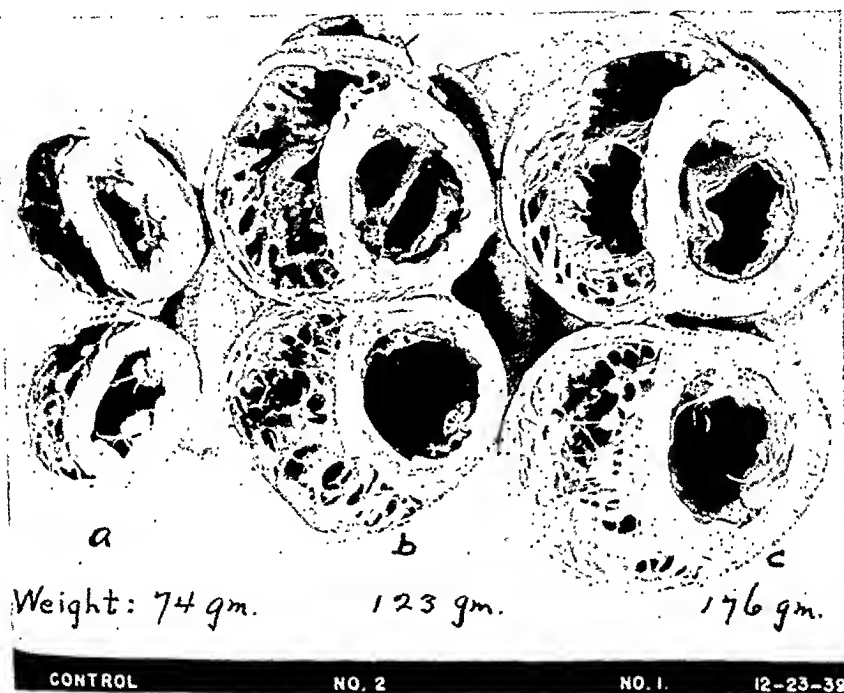


Fig. 9.—Cross-section of hearts of three litter mates: *a*, Control animal; *b*, pup with aorta-vena cava fistula 12 mm. in circumference; *c*, pup with aorta-vena cava fistula 18 mm. in circumference. The cardiac dilatation and hypertrophy were commensurate with the size of the fistulas.

The extraordinary dilatation and hypertrophy of the heart consecutive to these fistulas in the growing animal contrast somewhat with previous observations in adult animals. In the latter instances the enlargement seemed to be mainly a dilatation, although hypertrophy also occurred to a minor degree. In Pup 1 three months after establishing the aorta-vena cava fistula, evidences of relative cardiac insufficiency were present, such as great dyspnea in the presence of a greatly enlarged heart. The enlargement up to this time was probably mainly due to dilatation. Six months later the animal was much less dyspneic and was in better general condition. The heart, however, was even larger than before, and at necropsy an astonishing hypertrophy was present (Fig. 9). The probable explanation is that

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recovered its previous size; there was a good femoral pulse to be felt in both groins, and the pulse rate was 200. The animal continued in good health until Oct. 27, 1939. On this date, the heart had increased greatly in size, although not as much as the heart of the litter mate (Figs. 7 and 9). The pulse rate was 140. A good femoral pulse could be felt on both sides, and there was no edema. The fistula was exposed and compressed, causing a fall in pulse rate from 140 to 104.



Fig. 8.—Roentgenograms of three litter mates following infection of circulatory system with bismuth oxychloride. *a*, Normal heart, aorta, and vena cava of control animal; *b*, moderate dilatation of heart, aorta, and vena cava following establishment of aorta-vena cava fistula at *f*, which at death proved to be 12 mm. in circumference; *c*, great dilatation of heart, aorta, and vena cava incident to fistula at *f*, 18 mm. in circumference. These infections prove that the dilatation involves the entire circulatory system through which the short-circuited blood passes; namely, the aorta from heart to fistula, the vena cava from fistula to heart, and all chambers of the heart.

Concomitant with the increase in the volume or bulk of blood flowing through the shorter circuit, attracted and diverted into it by reason of the decreased peripheral resistance in this circuit, another important compensatory phenomenon comes into play. In the immediate period following the opening of the fistula, the diversion of blood into the fistulous circuit abstracts blood from the general circulation with a marked concomitant fall in blood pressure. To compensate for this diversion and to restore a normal blood pressure to the general circulation, an increase in total blood volume occurs, which is large or small, depending upon the size of the fistula.¹⁰

The following observations on total blood volume in these three litter mates were made:

| ANIMAL | DATES | WEIGHT | BLOOD VOLUME |
|---------|---------|----------|--------------|
| Control | 2/23/39 | 10.4 kg. | 950 c.c. |
| | 8/23/39 | 11.6 kg. | 960 c.c. |
| Pup 2 | 2/28/39 | 10.5 kg. | 1,190 c.c. |
| | 9/20/39 | 10.7 kg. | 1,210 c.c. |
| Pup 1 | 2/23/39 | 10.0 kg. | 1,430 c.c. |
| | 8/23/39 | 11.1 kg. | 1,550 c.c. |

By mathematical computation from measurements obtained in the roentgenograms of the injected animals (Figs. 8 and 10), the following approximate capacities were determined for that part of the circulatory system included in the shorter fistulous circuit, including the heart, the aorta from heart to fistula, and the vena cava from fistula to the heart:

| CAPACITY | TOTAL BLOOD VOLUME | INCREASE IN CAPACITY AS COMPARED TO CONTROL | INCREASE IN TOTAL BLOOD VOLUME AS COMPARED TO CONTROL |
|----------|--------------------|---|---|
| Control | 200 c.c. | 960 c.c. | |
| Pup 2 | 480 c.c. | 1,210 c.c. | 250 c.c. |
| Pup 1 | 775 c.c. | 1,550 c.c. | 590 c.c. |

In these three litter mates, equal in weight and stature (Fig. 10), there was a surprising correlation between the increase in capacity of the shorter circuit and the increase in the total blood volume, both being commensurate with the size of the fistula. It may be inferred that, if no demonstrable dilatation of the heart or of the vessels proximal to the fistula occurs, there is probably also no demonstrable increase in blood volume. I believe that even small fistulas are accompanied by a minor dilatation of the heart and vessels and by commensurate increases in total blood volume, but our methods are not exact enough and our eyes not keen enough to demonstrate and to recognize such minor dilatations and such small increases in blood volume. It is freely granted that the dye method is not a very ac-

in the intervening months hypertrophy had "caught up" with the previous dilatation. It is suggested that, when dilatation outstrips hypertrophy, relative decompensation occurs; when hypertrophy parallels dilatation, enormous enlargement may occur without decompensation.

Various authors,^{6, 7} following the lead of Lewis and Drury, have ascribed the enlargement that occurs in an arteriovenous fistula mainly to a dilatation consecutive to a "deficient nutrition of the heart muscle consequent on the fall of mean arterial pressure." It is obvious that the degree of cardiac hypertrophy demonstrated in these growing animals is not compatible with a deficient nutrition of the cardiac muscle. Since it has been conclusively demonstrated that the dilatation involves the entire part of the circulatory system through which the short-circuited blood passes, including all chambers of the heart, and the artery and vein between the fistula and the heart, it can be dogmatically stated that the cardiac enlargement and the dilatation of the vessels are both due to the same cause; namely, to an increased bulk or volume of blood flowing through the shorter circuit. As Porter⁸ ably states: "The enlargement of the artery and vein in the fistulous circuit and the increase in cardiac size are primarily an adjustment dilatation. There is a great increase in cardiac filling due to acceleration of the velocity of blood flow, and increase of effective venous pressure in the involved vein."

It has been repeatedly demonstrated that cardiac output is greatly increased and even doubled in the presence of a moderately sized fistula,⁹ and numerous observations indicate that there is an increase in venous pressure in that part of the venous bed lying between a fistula and the heart. Although contrary to the conclusions of Lewis and Drury, these are established facts. It has never been contended that there is a "marked rise in general venous pressure," but that there is a rise in venous pressure proximal to a fistula, the extent of which depends upon the size and duration of the fistula, cannot be questioned.⁸ When a fistula is opened, the increased velocity of flow through the vena cava may greatly increase the volume of blood delivered to the heart, and an efficient, undecompensated heart can effectively propel forward a greatly increased volume of blood delivered to it without a rise in general venous pressure, or even without much rise in lateral vena caval pressures. Porter concludes that "with adjustment dilatation of the artery and vein, the rate of the blood flow and the pressure in the vein decrease while the cross-section of the column of the returning circuit increases." It is apparent that the thin-walled, easily distensible vena cava lying free in a large cavity is capable of great adjustment dilatation, and a great increase in effective venous pressure at the portal of the heart may occur without necessarily increasing the general venous pressure.

curate method of studying blood volume, but one cannot ignore these results obtained in animals of the same litter on successive occasions, nor can one escape the fact that if there is a considerable increase in the capacity of the circulatory system by dilatation, there must be an increase in blood volume to fill it.

THE EFFECTS OF BILATERAL FEMORAL FISTULAS

On Arterial Pressures.—In an animal in which bilateral femoral fistulas had been established on Oct. 31, 1934, the following observations (Fig. 12) were made on June 28, 1938. Under nembutal anesthesia

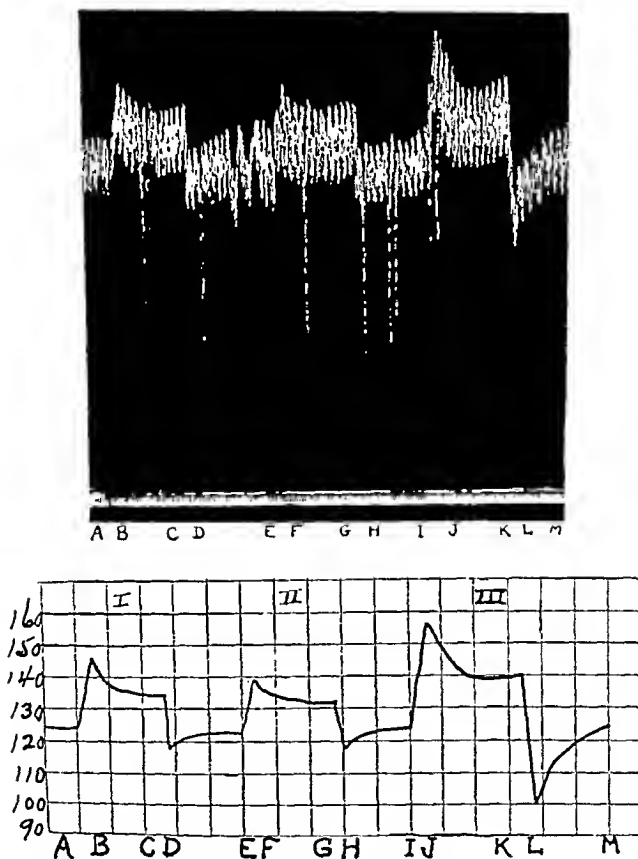


Fig. 12.—Kymographic record of carotid blood pressure in the presence of bilateral femoral fistulas. A, Both fistulas open; pulse, 102; B, C, right fistula closed; pulse, 87; D, E, both fistulas open; pulse, 98; F, G, left fistula closed; pulse, 82; H, I, both fistulas closed simultaneously; pulse, 76; J, K, both fistulas opened simultaneously. The effects upon blood pressure and pulse depend upon amount of blood diverted into the venous bed.

and with aseptic precautions, the right carotid artery was cannulized and both fistulas in the groin were exposed to permit complete closure of the artery proximal to the fistula. On closing the right fistula, the blood pressure rose immediately from 124 (pulse, 102) to 146 mm. Hg, dropping to a level of 136 mm. Hg (pulse, 87) as long as the fistula

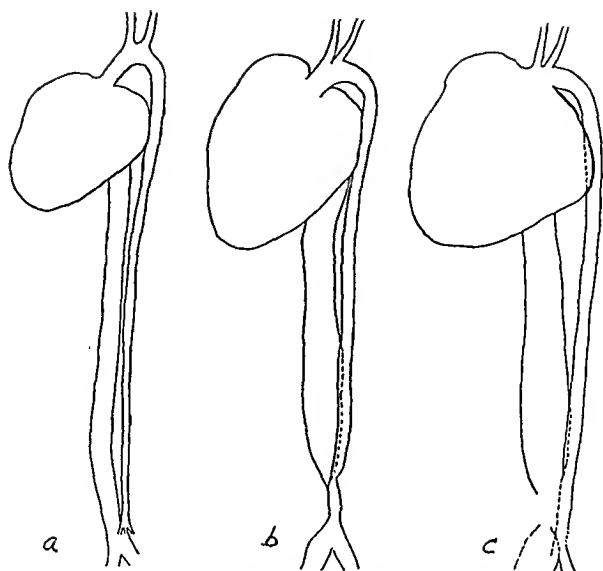


Fig. 10.—Tracings of injected specimens (Fig. 12) to illustrate dilatation and, therefore, increased capacity of that part of the circulatory system through which the blood short circuited by the aorta-vena cava fistula flowed. By mathematical computation the capacity of this part of the circulatory system was as follows: *a*, Control, 200 c.c.; *b*, Pup 2, 480 c.c.; *c*, Pup 1, 775 c.c.

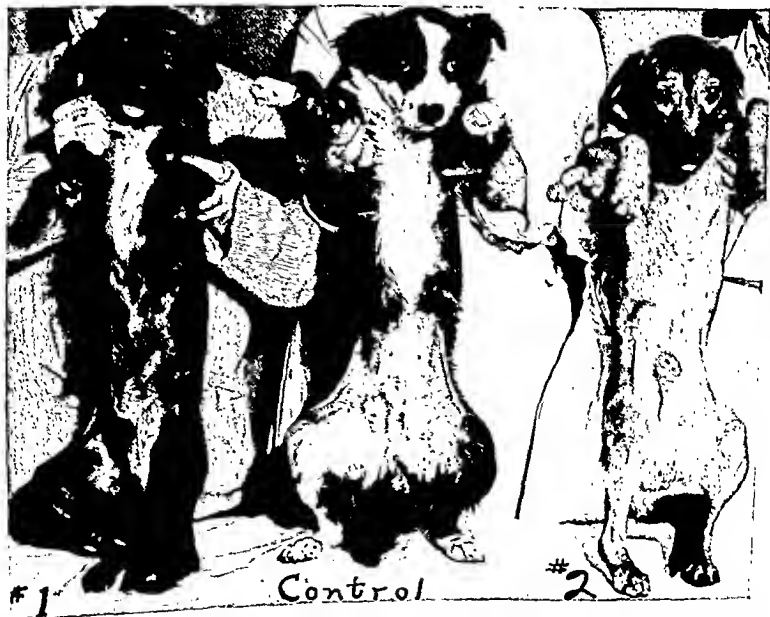


Fig. 11.—Photograph of three litter mates. Dogs 1 and 2 having aorta-vena cava fistulas. Dog 1: Weight, 11.1 kg.; blood volume, 1,430 c.c. Dog 2: Weight, 10 kg.; blood volume, 1,210 c.c. Control: Weight, 11.6 kg.; blood volume, 960 c.c.

of the aorta, becomes overdistended by the volume of blood by which the normal volume has been augmented since the introduction of the fistula. This overdistention causes a sudden and excessive, though temporary, increase in blood pressure, which is promptly rectified, so far as it is possible, by a general vasodilatation and, through the vagus, by a reduction in the rate of cardiac contractions. As a result, after two to three beats the blood pressure drops to a lower level, though it is still higher than when the fistula is open. A part of the increase in blood pressure is due, of course, to raising the peripheral resistance, but were it due solely to the elimination of an area of lessened resistance there would be a flat curve without the few initial beats of very high pressure. Indeed, the flat type of curve is obtained when a fistula is first established, before the blood volume has increased: Opening the fistula drops the blood pressure to lower diastolic and systolic levels; closing the fistula restores blood pressure to the previous levels, these changes being entirely due to reducing and increasing peripheral resistance.

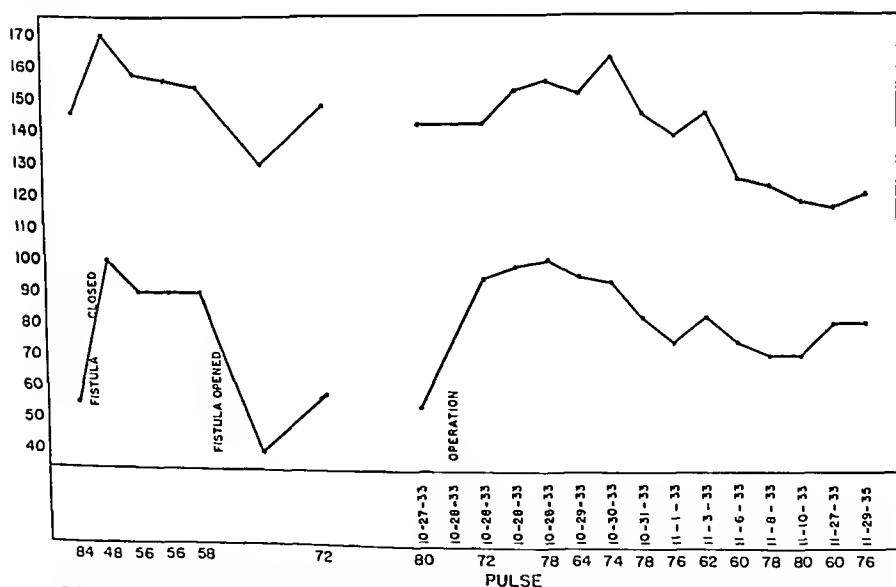


Fig. 14.—Variations in blood pressure incident to closure of a common femoral fistula of four years' duration, (a) By digital pressure; (b) by operative elimination. The blood volume decreased from 7,200 to 6,200 c.c. following operative removal of the fistula.

When a large fistula of long duration is permanently eliminated, the blood pressure curve also takes on a very characteristic form (Figs. 13-15). There is again a temporary increase both in diastolic and systolic pressures which then gradually subside to lower levels, the diastolic remaining permanently elevated, the systolic approximately the same as before the closure of the fistula. These transient increases can be explained only on one basis: the overdistention of the normal arterial bed by an abnormally large volume of blood which

remained closed. On opening the fistula, the blood pressure dropped precipitately to 118 mm. Hg, rising promptly to a level of 122 mm. Hg as long as the fistula remained open. Similar figures were obtained on closing the left fistula (Fig. 12). On closing both fistulas simultaneously, the pressure rose preeipitately to a high point of 156 mm. Hg (pulse, 76), dropping to a level of 140 mm. Hg as long as the fistula remained closed. On opening the two fistulas simultaneously, the pressure dropped to a low point of 100 mm. Hg for several beats only, rising promptly to the previous level of 124 mm. Hg.

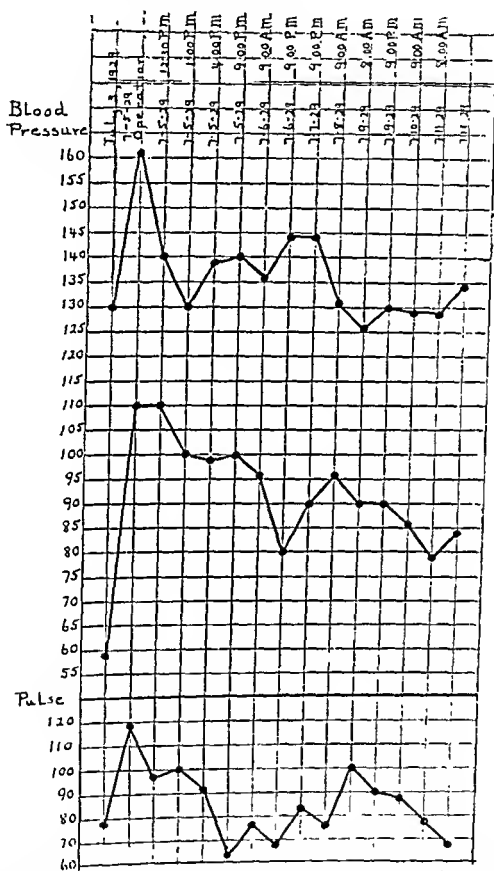


Fig. 13.—Variations in general blood pressure following the removal of a large carotid-jugular fistula of eighteen months' duration. For forty-eight hours, both systolic and diastolic pressures were excessively elevated due to overdistention of circulatory system by the increased blood volume that occurred in the presence of the fistula. Following operation, the total blood volume decreased from 8,900 to 7,800 c.c.

It was a convincing demonstration of the fact that the physiologic effects of opening and closing a peripheral fistula depend upon the volume of blood escaping into the shorter circuit.

The form of the blood pressure curve obtained on closing a fistula of long duration is unique and distinctly characteristic. Closing the fistula forces into the arterial bed the blood formerly leaking into the capacious venous system. The normal arterial tree, including the arch

It was apparent that the vena cava was able to accommodate much of the increased volume of blood transmitted through the fistula under arterial pressure by an increased velocity of flow. However, it was also apparent that the vena caval pressure varied directly with the volume of blood diverted through the fistulas, being greatest with both fistulas open, least with both fistulas closed; intermediate rises in vena caval pressure occurred as one or the other fistula was opened separately.

On March 19, 1940, a second dog (Animal 3), in which bilateral femoral fistulas had been established on June 30, 1938, was investigated as to vena caval pressures. Under morphine and ether, a long glass cannula was introduced through a rent in the left external jugular vein down into the thoracic vena cava. This experiment differed from the preceding experiment in that both the abdomen and the thorax were intact. The following observations were noted, the vena caval pressures oscillating 5 to 10 mm. with respiration:

| | VENA CAVAL PRESSURE IN CM. OF WATER | PULSE |
|-----------------------|--|-------|
| Both fistulas open | 9.5-10 | 108 |
| Right fistula closed | 6.5-7 | 90 |
| Left fistula closed | 7.5-8 | 96 |
| Both fistulas closed | 5.5-6 | 88 |
| Left fistula reopened | 7.5-8 | |
| Both fistulas open | 9.5-10.5 | |

Again, it was demonstrated that vena caval pressure was increased in the presence of bilateral femoral fistulas, the greatest increase occurring when both fistulas were open. Closing one or the other fistula lowered the venous pressure 2 to 3 cm.; whereas, closure of both fistulas simultaneously lowered it 4 cm.

On March 4, 1940, the dog in which two femoral fistulas had been established on Oct. 31, 1934, was again anesthetized; the remaining left renal vein was cannulized for vena caval pressures, and the remaining left carotid artery was cannulized for arterial pressures (Fig. 16). It is evident from the kymographic record that, when both fistulas were open, the vena caval pressure was high and carotid pressure was low; when both fistulas were closed, vena caval pressure was low and carotid pressure was high. Intermediate arterial and vena caval pressures were obtained, depending on closure of one or the other fistula.

From these many observations one may conclude (1) that a rise in venous pressure occurs proximal to an arteriovenous fistula, and (2) that the extent of this rise in venous pressure depends upon the amount of blood diverted into the shorter circuit, which is determined by the size of the fistula.

requires several days for reduction and readjustment to the new conditions incident to the elimination of the fistula. The permanent elevation of diastolic pressure is secondary to the elimination of an area of decreased resistance.

The concept of an increase in total blood volume provides a logical and acceptable solution for the variations in blood pressure and pulse that characterize the opening and closing of the peripheral arterio-venous fistula.

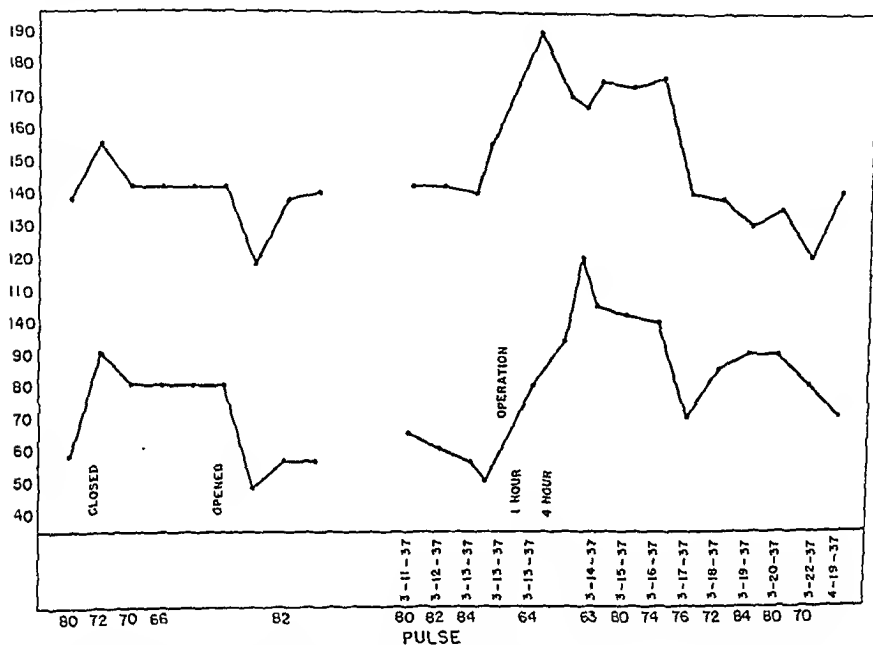


Fig. 15.—Variations in blood pressure incident to closure of a superficial femoral fistula of five years' duration. (a) By digital pressure; (b) by operation. The blood volume decreased from 5,040 to 4,200 c.c. following elimination of the fistula.

On Vena Caval Pressures.—On April 14, 1939, the animal in which bilateral femoral fistulas had been established three and one-half years previously was again subjected to nembutal anesthesia and under aseptic precautions the following procedures were carried out: Through an incision in the flank the right kidney was mobilized, the renal artery was ligated, and a glass cannula connected with an upright glass tubing of equal caliber was inserted into the vena cava through the renal vein. The pressure, oscillating with respiration, was recorded in centimeters of water under the following conditions:

| | VENA CAVAL PRESSURE IN CM. OF WATER | | |
|----------------------|--|-----------|-----------|
| Both fistulas open | 12-13 | 17-18 | 19-20 |
| Right fistula closed | | | 16.5-17.0 |
| Left fistula closed | 10-11 | 15-16 | |
| Both fistulas closed | 8.5-9 | 12-13 | 15-15.5 |
| Both fistulas open | 12.5-13 | 15.5-16.5 | 18.5-19 |

A marked decrease in cardiac size also accompanies hemorrhage, the diminution in the size of the heart being commensurate with the degree of blood loss.

The size of the heart conforms accurately to the volume of blood flowing through it.

The dilatation that accompanies an arteriovenous fistula is not restricted to the heart, but affects the vessels involved in the fistulous circuit. The same cause is responsible for both dilatations; namely, an increase in the volume or bulk of blood flowing through that part of the circulatory system through which the blood short circuited by the fistula must flow; i.e., all the chambers of the heart, the proximal artery, fistula, and the proximal vein.

In the growing animal the dilatation may be very great without evidence of decompensation and may be accompanied by pronounced hypertrophy. It is suggested that, when dilatation outstrips hypertrophy, decompensation occurs; when dilatation is paralleled by an equivalent hypertrophy, great enlargement and dilatation of the heart may occur without decompensation.

In a crucial experiment involving three litter mates of equal weight and stature, one acting as control, one having an aorta-vena cava fistula 12 mm. in circumference, and one having an aorta-vena cava fistula 18 mm. in circumference, there occurred an increase in blood volume commensurate with the size of the fistula.

In the same animals an increase in the capacity of the circulatory system occurred, also commensurate with the size of the fistula. The increase in capacity and the increase in blood volume closely paralleled each other.

In an animal with bilateral femoral fistulas the increase in blood pressure and reduction in pulse rate were greatest when both fistulas were closed simultaneously, and considerably less when either fistula was closed separately. The physiologic effect of a fistula, therefore, clearly depends upon the volume of blood diverted through the fistula, which is determined by its size.

The transient high systolic and diastolic pressures that persist for several days following operative closure of a fistula are due to the increase in blood volume that has occurred during the existence of the fistula. The permanent elevation of diastolic pressure is secondary to the elimination of an area of decreased peripheral resistance.

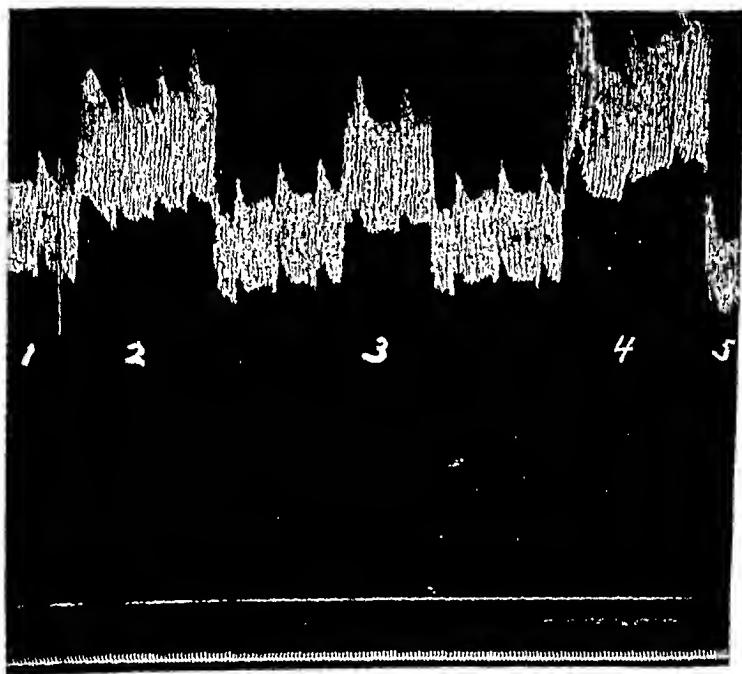
In animals having bilateral femoral fistulas, vena caval pressures were highest with both fistulas open, least with both fistulas closed, and intermediate pressures were obtained on closing one or the other fistula separately. Venous pressures proximal to a fistula are determined by the volume of blood diverted through the fistula and therefore by the size of the fistula.

SUMMARY

In the first twenty-four to forty-eight hours after the establishment of a large arteriovenous fistula, the heart diminishes in size, followed, if the animal survives, by a prompt return to normal, and, subsequently, by a gradual dilatation which may be apparent within four to five days.

Death due to an excessive diversion of blood through the fistula may occur, accompanied by a marked diminution in cardiac size.

A marked diminution in cardiac size accompanies shock.



| Conditions at Site of Fistulae | Mean Arterial Pressures Carotid Artery mm. Hg. | Vena Caval Pressures cm H ₂ O |
|-----------------------------------|---|--|
| 1. Both Open | 136 | 13 — 15 |
| 2. Left Closed | 160 | 9 — 10.5 |
| 3. Right Closed | 156 | 8.5 — 10 |
| 4. Both Closed | 182 | 6 — 7 |
| 5. Both Open | 120 | 13 — 14 |

Fig. 16.—Kymographic record of carotid arterial pressures dependent upon conditions at site of bilateral femoral fistulas of five and one-half years' duration. Vena caval pressures obtained by cannulization of renal vein.

PROGRESSIVE LYMPHEDEMA ASSOCIATED WITH RECURRENT ERYSIPELOID INFECTIONS

ALTON OCHSNER, M.D., ALFRED B. LONGACRE, M.D., AND
SAMUEL D. MURRAY, M.D., NEW ORLEANS, LA.

(From the Department of Surgery, School of Medicine, Tulane University)

DISCUSSING elephantiasis, Matas^{1, 2} first in 1911 and later in 1913 described the similarity of the clinical picture of recurrent erysipelas and that of the acute attacks of recurrent lymphangitis occurring periodically in cases of progressive lymphedema which terminate in elephantiasis. Since these publications, many clinical and experimental reports concerning the etiology and pathogenesis of this disease have been made. Much of the evidence tends to support secondary infection, principally that of streptococcus, as a major etiological factor. However, these investigations do not establish a definite etiology and, as a result, the present methods of treatment remain empirical and have not proved entirely satisfactory.

ETIOLOGY

Reporting the demonstration of the ova and worms of *Filaria bancrofti* in the lymphatics and lymph glands of patients with tropical elephantiasis Manson³ in 1898 re-emphasized in the production of this disease the importance of an inflammatory obstruction of the lymphatic system resulting from infection by filaria. As a result of this report, elephantiasis was for a long time considered a disease of the tropics resulting from an infestation of the lymphatics and lymph glands with filaria. However, it was not long before there appeared reports of cases of elephantiasis in patients who had at no time been in the tropics. The progressive development of lymphedema, with associated attacks of acute lymphangitis, as well as the end stage of the elephantoid condition were essentially the same in both the tropical and nontropical varieties of this disease. The reports of these sporadic cases immediately opened to question the role of filaria as the only etiological agent in this disease. Cases occurring in the tropics in patients who give no history of filariasis and in whom the filaria organism cannot be demonstrated make exceedingly doubtful the specificity of filaria as an etiological agent even in tropical cases.

In discussing the etiology of this disease, one must constantly bear in mind the similarity of the attacks of acute lymphangitis to those of recurrent erysipelas. Because of this similarity, the possibility of a common etiologic factor's being responsible for both erysipelas and the acute exacerbations in elephantiasis must be considered. In 1883 Fehleissen⁴ reported the successful isolation and culturing of streptococci in skin lesions in cases of erysipelas. In addition to the isolation

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coccal infections. These observations plus the disappearance of reactions following desensitization of the involved tissue by means of the injection of increasing doses of toxin indicate a local tissue sensitivity. In other words, following an initial streptococcal infection, the tissues may become sensitive to the toxins and metabolic products of these organisms and therefore will react in a similar manner to these toxins and metabolites as in the original infection. These observations offer a possible explanation for the recurrent attacks of erysipelas resulting from foci of infection in more distant tissues.

Hutchinson¹⁹ in 1904 stated that whatever causes an obstructive inflammation of the lymphatic trunks may in dependent parts produce elephantoid hypertrophy. This statement aptly describes the pathogenesis of the disease under discussion, but it does not establish definite etiology of the obstructive inflammation. Sabouraud²⁰ in 1892, followed by Moncorvo²¹ and Unna²² in 1896, reported the demonstration of streptococcus in patients with recurrent erysipelas and elephantiasis. They believed that the recurrent inflammation of the lymphatics resulting from an infection by the streptococcus was responsible for the production of nontropical elephantiasis. Unna²² emphasized the importance of the inflammatory exudate in addition to simple obstruction in producing fibromatosis characteristic of elephantiasis. He explains the periodic occurrence on the basis of incomplete healing of the original lesion resulting in a vascular disturbance and the incomplete destruction of the streptococci. As suggested by Matas,^{1, 2} there are probably many cases of tropical elephantiasis in which the filaria plays no part but which are the result of repeated infections of the lymphatic system by pyogenic organisms.

The above opinions are corroborated by the observations made in the tropics by several workers who reported numerous cases of elephantiasis in which there was no history of filaria and in which filarial organisms could not be demonstrated. In 1921 Rose,²³ by an analysis of previous reports of Grieve²⁴ (1883), Conyers and Daniels²⁵ (1886), Daniels and Castellani²⁶ (1908), and of his own statistics (1920), showed the incidence of elephantiasis in British Guiana to vary between 3.9 and 19.2 per cent; whereas, the incidence of clinical filariasis was between 14.8 and 25.3 per cent. He further showed that secondary infection by bacteria plays an important part in the production of elephantiasis in the tropics, stating that one can recover a pure culture of streptococcus in 90 per cent of the cases of elephantiasis from the "juice" or pus from the acutely inflamed regional lymph glands. In other cases he found a mixture of organisms, including streptococcus, *Staphylococcus albus*, *Bacillus coli*, and *B. pyocyaneus*. In 1908 Powell²⁷ was unable to demonstrate filaria in any of seven cases afflicted with elephantiasis in Bombay. He found 5 per cent of a large number of inhabitants examined for filariasis to be infected with the organism, yet free from elephantiasis. Megaw²⁸ in 1908 reported that

of the organism, he reproduced erysipelas with pure cultures of streptococcus in seven persons suffering from malignant growths. He also fulfilled the principles laid down by Koch which are necessary to demonstrate the specificity of an organism in a disease by reproducing the disease in animals and successfully recovering the organisms from them. Shortly after this report of Fehleissen,⁴ numerous other workers reported cases of erysipelas from which they isolated various other organisms; i.e., staphylococci and pneumococci. In some instances these other workers offered experimental reproduction of erysipelas in animals as evidence that their organisms were capable of producing erysipelas. However, these investigations were never conclusive and have never seriously challenged the role of the streptococcus as the etiologic agent in cases of erysipelas. At present it is conceded that erysipelas is the direct result of an infection by streptococci.

In more recent years attention has been focused on the study of the specificity of strains of streptococci recovered from cases of erysipelas as compared to the strains recovered from other streptococcal infections, principally that of scarlet fever. By means of agglutination, agglutinin absorption, and in vivo experiments with homologous and other strains of streptococci isolated from cases of erysipelas and with streptococci recovered from cases of scarlet fever, Birkhaug⁵⁻⁸ and Eagles^{9, 10} demonstrated definite evidence of specificity of strains recovered from cases of erysipelas. Similar experiments by Gay and Morrison¹¹ did not confirm this specificity. Because of this conflicting evidence, an attempt was made to demonstrate the specificity of these strains of streptococci by studying toxin and antitoxin reactions of the various strains. Subsequent in vitro and in vivo neutralization experiments with toxin and antitoxin by Birkhaug,⁵⁻⁸ Dick and Dick,¹² Andrewes,¹³ and Stevens and Dochez¹⁴ suggest the possibility of the specificity of the strains of streptococci recovered from cases of erysipelas. On the other hand, Singer and Kaplan¹⁵ were unable to confirm the results of Birkhaug⁵⁻⁸ and others with neutralization experiments and concluded that the streptococci of scarlet fever and erysipelas were not biologically specific. Because of the lack of uniformity of the results of these experiments, at the present one must conclude that erysipelas is caused by hemolytic streptococci which may or may not be specific for this disease.

Stevens and Dochez,¹⁴ Stevens,¹⁶ and Francis,¹⁷ by means of skin tests performed both during the acute phase of and in the convalescence from the disease, were able to demonstrate a local tissue sensitivity to metabolic products from cultures of streptococci recovered from cases of erysipelas. Stevens¹⁶ compared these focal reactions to reactions seen in tuberculous patients following the injection of tuberculin. Amoss¹⁸ observed similar reactions in a child with staphylococcus infection resulting from the injection of a staphylococcus filtrate of the organism recovered from the patient. Stevens¹⁶ produced focal responses with homologous streptococcal filtrates in patients suffering from strepto-

coccal infections. These observations plus the disappearance of reactions following desensitization of the involved tissue by means of the injection of increasing doses of toxin indicate a local tissue sensitivity. In other words, following an initial streptococcal infection, the tissues may become sensitive to the toxins and metabolic products of these organisms and therefore will react in a similar manner to these toxins and metabolites as in the original infection. These observations offer a possible explanation for the recurrent attacks of erysipelas resulting from foci of infection in more distant tissues.

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progressively accumulating mass of evidence in favor of an etiologic pyogenic infection, there are undoubtedly cases of elephantiasis which can be explained solely as a result of filarial infection. However, the evidence indicates that even in tropical elephantiasis the role of secondary infection is assuming major proportions.

As mentioned previously, Sabouraud²⁰ and Unna²² were the first to call attention to the possible etiologic significance of streptococci in cases of progressive lymphedema associated with erysipelas-like attacks. It is upon such evidence that the etiology in the nontropical variety of elephantiasis can be established. In 1921 Halsted,³³ in discussing lymphedema following radical mastectomy, demonstrated that radical excision of the axillary glands or axillary vein or both will not in themselves produce this condition. There must be, in addition to the interference with lymphatic and blood flow, a secondary infection in order to produce elephantiasis of the upper extremity. Sistrunk³⁴ in 1921 reported 33 cases of elephantiasis, 9 of which were proved definitely to be the result of some infection in various types of wounds. He failed to mention whether or not cultures were obtained. Reichert³⁵ in 1929 made the following statement: "Simple lymphedemas are the result of stasis. Add the factor of infection, and we have an entirely different picture, that of elephantiasis. Chronic infection, usually caused by streptococcus, after a time readily leads to a progressive hypertrophy of the hypodermal and dermal connective tissues. Simple mechanical blockage of the lymphatics causes regional lymphedema but the characteristic fibromatosis and histological changes peculiar to the elephantoid states cannot be produced without pyogenic infection." Kuntzen³⁶ in 1930 stated that lymphatic obstruction plays the major role, erysipeloid streptococcal infection being secondary in the production of elephantiasis and pyogenic infection acting only to intensify the course of the disease. Castellani^{37, 38} in 1934, in addition to *Staph. aureus* and *Staph. albus*, *Staph. viscidus*, and hemolytic and nonhemolytic streptococcus, found two rare coccobacilli, *Micrococcus meta-mycticus* and *M. micromycticus*, in cases of nonfilarial elephantiasis. More recently, Tisseuil,³⁹ Gougerot and Vial,⁴⁰ and Telford and Simmons⁴¹ report other cases of elephantiasis which probably resulted from pyogenic infection.

Supporting the clinical evidence that streptococcus plays a major etiologic role in the production of elephantiasis is the work of Homans,⁴² Drinker, and their co-workers.⁴³⁻⁴⁶ They were able to reproduce typical lymphedema in dogs by injecting a mixture of quinine and silica into the lymphatics. One of these dogs developed spontaneously an acute illness which in many respects resembled cases of recurrent erysipelas or exacerbations of lymphangitis. From material aspirated from the edematous limb during the acute attacks, cultures of streptococci were obtained which, when injected into a normal dog, failed to produce a lesion but which, when injected into an edematous limb, reproduced a similar attack. These workers suggest that, even though streptococci

of 100 prisoners examined only 3 had elephantiasis; whereas 15 of the entire number were found to be infected with filaria. The three patients with elephantiasis gave no history of filarial infestation and the larvae could not be demonstrated in their blood on repeated examinations. Dubruel²⁹ in 1910 concluded that the tropical form of elephantiasis is more closely allied to the sporadic form and should be considered contagious during the attacks of erysipelas. His conclusions are based on the examinations of the inhabitants of the island of Morrea where about 12 per cent of the population have elephantiasis, yet he was able to demonstrate filaria in only 1 case; whereas, in many he found streptococcus in pure culture. He failed to state the areas from which these cultures were obtained. In 1930 Suarez³⁰ reported the study of 60 cases of recurrent lymphangitis associated with elephantiasis of the lower extremities. Cultures obtained from subcutaneous tissues in 50 patients were negative in all but 2 cases in which streptococci were found. In the remaining 10 cases cultures were made from septic foci; the hemolytic streptococcus was cultured in 9 and the hemolytic *Staph. aureus* in 1. Repeated examinations for microfilaria in the blood were negative in all of these cases. Croll stated that 11.5 per cent of 4,000 Europeans admitted to Brisbane Hospital in Australia showed filarial infection, but none had the symptoms of elephantiasis. McKinley,³¹ in attempting to repeat Suarez' work,³⁰ obtained cultures by aspiration of the subcutaneous tissues in 27 patients, in none of whom was there any growth. Of 9 additional cases in which cultures were taken from ulcers or other septic foci, hemolytic streptococci were found in 7 instances and hemolytic *Staph. aureus* in 2. In 11 other patients he obtained cultures from sections of the skin and found the green streptococcus in 1 and the hemolytic *Staph. aureus* in another. The inconsistency of these findings led him to believe that bacterial infection does not always or even commonly play a role in acute filarial lymphangitis and that it is possible to have acute lymphangitis of filarial origin without bacterial invasion. In 1932 Acton and Rao³² suggested the following two possibilities by which filaria can produce lymphatic obstruction: (1) by chronic inflammation and obstruction resulting from repeated and prolonged damage to the lymph glands by the passage of the larvae through them; (2) by an acute inflammatory change in and around the glands which have been damaged previously by the larvae, this inflammation usually being caused by pyogenic cocci. These hypotheses of Acton³² are unusually interesting in that they offer a possible explanation why elephantiasis is more prevalent in the tropic than in the temperate zone. Matas^{1, 2} suggests that the mode of living of natives in the tropic zones continually exposes the skin to both minor and major injuries which serve as a portal of entry for pyogenic organisms. Both Matas and Acton maintain a neutral attitude in not trying to attribute all cases of elephantiasis to infections by either filaria or pyogenic organisms. This is particularly significant in that, in spite of the

crease and ultimately become negative. These tests were performed in cases of acute erysipelas and are mentioned only to illustrate and support the hypothesis of tissue sensitivity to streptococcal filtrates.

Numerous authors have reported various conditions which produce lymphedema which in some instances progress to the elephantoid state. As this paper is concerned only with the type resulting from periodic recurrent attacks of lymphangitis (erysipeloid), no other will be considered. The summary of the various factors which have been suggested as causing these attacks which result in the typical elephantoid limb may be classified as follows: (1) filarial; (2) filarial plus pyogenic infection; (3) lymphatic obstruction other than filarial plus pyogenic infection; (4) pyogenic infection (streptococcal); (5) local tissue sensitivity: (a) metabolic products of streptococci; (b) trichophyton.

PATHOGENESIS

In order to understand more clearly the pathogenesis of this disease, it is important to review the anatomy and the physiologic functions of the lymphatic system. In general the lymphatic system consists of anastomosing networks of capillaries which in turn drain into larger lymphatic trunks, which are interrupted in various places by interposed lymph glands. These glands have both afferent and efferent vessels, the latter emptying the lymph into larger ducts and eventually into the thoracic ducts which terminate in the subclavian veins. The lymph capillaries consist of a closed system of vessels composed of a single layer of flat endothelial cells which are bathed in tissue fluid. Lymph capillaries are found in every organ possessing a blood vascular circulation. However, we are concerned only with the lymphatics of the connective tissues of the extremities; therefore a discussion of the lymphatics of the other organs will not be included. In the skin the capillaries are found in the dermis. According to Gray,⁵¹ the subcutaneous tissues are without capillaries but contain small lymphatic vessels. The capillary system of the muscles is not clearly understood, but it is generally conceded that muscle contains fewer plexuses of lymphatic capillaries than do the more superficial tissues. The osseous system, including the periosteum and bone proper, contain abundant capillaries. In the extremities the capillary systems are divided into two parts between which there is very poor, if any, connection. The superficial lymphatic system of the upper extremity, however, has many more communications with the deeper system than are found in the lower extremity. The superficial capillary system of the upper extremity empties into lymphatic vessels which follow the course of the superficial vascular tree and terminate in the epitrochlear and axillary lymph glands. The deep lymphatic system consists of capillaries which drain muscle tissues, intermuscular connective tissues, and the osseous system; these coalesce to form four sets of lymphatic trunks: (a) radial, (b) ulnar, (c) volar, and (d) dorsal. These four trunks follow the respective vessels of the deep circulation and terminate in the axillary glands.

may not be responsible for the initial lymphatic obstruction producing lymph stasis, lymph stasis predisposes the involved area to pyogenic infection. Prior to the work of Drinker,⁴³⁻⁴⁶ Homans,⁴⁷ and others, Reichert,³⁵ Homans,⁴⁷ and Homans and Zollinger⁴⁸ had attempted to reproduce lymph stasis in dogs by the simple blockage of lymphatics, by employing various techniques. In additional experiments Homans also ligated the femoral vein. By these methods they were able to produce only a transient lymphedema of approximately two to three weeks' duration and concluded that the failure to produce permanent edema probably was due to the rapid re-establishment of the severed lymph channels.

Various authors have suggested other etiologic agents as responsible for this disease. The demonstration of Sulzberger and co-workers⁴⁹ of a sensitivity to the trichophyton in the involved area is indicative that this fungus may be of etiologic significance in some of the cases. They offer as additional evidence the improvement resulting from desensitization to the trichophyton. Mulholland⁵⁰ states that many of the cases seen on the third surgical division of Bellevue Hospital of New York show a marked improvement with decrease in swelling once the epidermophytosis has been eradicated. Other authors, observing a similar relationship between epidermophytosis and elephantiasis, believe that elephantiasis is not a result of the epidermatophytosis but of infection by the streptococcus which in many instances can be isolated from cracks and fissures of the skin associated with the fungus infection.

In 1933 Stevens,¹⁰ in discussing chronic infectious edema, advanced the theory of local tissue sensitivity to the metabolic products of the streptococcus. From cultures which he obtained by aspirating the lesions, filtrates which he used for immunization were made. He would invariably reach a critical dose which would cause a reaction at the site of injection similar to that seen in exacerbations. Continued immunization caused a development of immunity to the toxin in much larger doses. The following quotation from Stevens¹⁰ is evidence to support this idea: "While impaired venous and lymphatic circulation is seen to be important in the pathogenesis, in the arm and leg, edema of the face has followed infections without similar predisposing circulatory disease—chronic infections of the sinuses have, however, appeared important in this respect. Four of five patients with facial edema had infected antra or ethmoidal sinuses. The importance of these infections is emphasized by the absence of similar infections among the fourteen patients in whom edema has not developed." In 1928 Francis¹⁷ reported results of skin tests done on 30 patients with sterile filtrates prepared from a culture of hemolytic streptococci obtained from a typical case of erysipelas; 20 cases during the active stage of the disease showed either no or only very slight reaction; whereas, 10 cases showed a definite response. Test doses repeated as the disease progressed toward convalescence showed a general tendency for sensitivity of the skin to increase instead of de-

mal conditions consist of about 95 per cent lymphocytes. Under conditions producing inflammatory reactions, the total cell count may increase, the additional cells consisting mainly of polymorphonuclear leucocytes.

Numerous workers have demonstrated that lymph stasis alone is not sufficient to produce the elephantoid condition. Unna²² and Sabouraud²⁰ contended that there must be a superimposed inflammatory reaction which keeps the cells bathed in the products of bacterial and cellular disintegration. If such is true, it is easy to understand why such conditions as congenital deformities or developmental abnormalities in lymphatic channels or tumors interfering with lymphatic flow or any other similar condition which interrupts the lymphatic passages may produce lymphedema without causing the changes characteristically found in the typical case of elephantiasis. Experiments to produce lymphedema, such as those of Homans⁴⁷ and Reichert,³⁵ which in brief consisted mainly of mechanically interrupting lymphatic trunks, blood vessels, or both, proved ineffectual in producing a permanent lymphedema, much less an elephantoid condition. Drinker and his associates⁴²⁻⁴⁶ were able to produce permanent lymphedema in dogs by the repeated injections of an irritating substance into the lymphatics. One or two of these dogs spontaneously developed an attack simulating the attacks observed in human beings. During this seizure they were able to isolate a streptococcus. Following the initial attack, spontaneous recurrences occurred periodically with a gradual increase in the size of the limb, more closely approaching that of elephantiasis. Clinically Halsted's³³ cases are similar examples in human beings.

The pathologic picture in a fully developed case of elephantiasis with its marked fibrous tissue proliferation is probably largely the result of increased protein content of interstitial fluids. This development of the elephantatic limb is gradual, occurring over a period of years. A cross section of a limb in a fully developed case shows a marked thickening of the derma and subcutaneous tissues. This thickening consists of an increase and hypertrophy of the fibrous tissue which extends to and occasionally involves the deep fascia. The underlying muscles usually show no changes, but occasionally they may be atrophic. Scattered throughout the fibrous connective tissues are dilated lymphatics which weep on cutting them. The blood vessel walls may show some thickening, but these changes are not as marked as are the other changes.

Irrespective of the inciting nature producing the initial lymph stasis, it is probably the inflammatory reaction with its exudative characteristics which causes the excess accumulation of proteins in the tissue fluid. A vicious circle is set up in that, in addition to the increased production of protein in the interstitial fluid from the inflammatory reaction, there is interference with the normal flow of lymph predisposing to excessive protein accumulation and fibrosis.

In the lower extremity the superficial lymphatics consist of anastomosing plexuses of capillaries in the dermis which coalesce to form lymphatic trunks in subcutaneous tissues. There are two sets of these lymphatic trunks; the median which follows the course of the great saphenous vein terminating in the femoral or subinguinal lymph nodes, and the lateral trunks which follow the lesser saphenous vessel to the popliteal lymph glands. It is in this region that there is a possible communication between the superficial and deep systems of lymphatics. As in the upper extremities, the deeper plexus drains similar tissues and its trunks follow the deeper vessels of the vascular system, terminating in the external iliac lymph nodes. Efferent vessels from the femoral and inguinal glands also drain into this group of nodes. The efferent vessels from the iliac nodes then communicate with the hypogastric and lumbar glands, finally terminating in the thoracic ducts, which empty into the subclavian veins.

The propelling forces producing lymph flow depend for the most part on two functions: the presence of arteriolar pulsations, as shown by McMaster and Parsons⁵² and by Cressman and Blalock;⁵³ and the active and passive contraction of skeletal muscles. In order to insure centripetal flow, the large lymphatic vessels contain valves which are attached to the vessel wall by the convex edges, the concave edges being free and in the direction of the current. These valves are lined by a single layer of endothelial cells. In most instances two valves of equal size are opposed to each other and they become more numerous as the lymphatic vessels approach the lymphatic glands. Factors increasing the flow of lymph besides the contraction of skeletal muscles and arteriolar pulsations include increased functional activity of the part by increased venous pressure or by general local hyperthermia. Allen⁵⁴ states that the rate of flow is modified but little, if any, by peripheral section of nerves or increased arterial pressure. Intravenous injections may cause increased flow of lymph by effecting the greater movement of fluid out of blood vessels or by injury to the capillary endothelium allowing proteinized fluid from the blood vessels to leak into the tissues. Any other factors causing increased capillary permeability, such as inflammation, may also accelerate the flow of lymph. Another factor increasing capillary permeability is a relative anoxia of the endothelium produced by decreased circulation resulting from arteriolar spasm.

The composition of lymph is similar to that of plasma in that it contains the same constituents of plasma but in a more diluted form. The specific gravity of lymph is approximately 1.015. According to Lowenberg,⁵⁵ the protein content of tissue fluid under normal conditions is approximately 1 per cent. Allen⁵⁴ in an analysis of dog's lymph found the protein content to be between 0.5 and 1.84 per cent. In addition to protein lymph contains nonprotein nitrogen, urea, creatinine, sugar, chlorides, fibrinogen, prothrombin, leucocytes, amino acids, phosphorus, and calcium. The cellular constituents of lymph under nor-

ened walls. Recently, attention has been focused on the alterations in the lymphatic system. Descriptions of these changes differ, some authors describing marked dilatation of lymph capillaries and smaller lymph vessels, others describing lymph soaked tissues in which they can find no evidence of existing lymphatic channels. Almost all authors agree that there are distinct areas showing coagulation of lymph within the lymph vessels. The changes occurring in the skin consist of a thinning of the epidermis with a thickening of the dermis. Occasionally a thickened epidermis showing hyperkeratosis has been described. The hair follicles disappear and the sweat glands show some degree of hypertrophy; collagen fibers of the subcutaneous tissues are swollen and are arranged in parallel bundles. The bundles, and in places the individual fibers, are widely separated by edema fluid. The overproduction of fibrous tissue replaces much of the adipose tissue and connects the skin with the thickened deep fascia. Elastic fibers, if present, are arranged in frayed bundles in which the individual fibers may be broken. Most authors state that there is a disappearance of elastic fibers. There is some disagreement as to changes observed in the blood vessels, but a thickening of the vascular wall is mentioned by many. The perivascular tissues show a slight round-cell infiltration.

CLINICAL MANIFESTATIONS

The prominent features of this disease during acute exacerbations in many respects resemble those of erysipelas. The attacks are usually ushered in by a feeling of dull pain which rapidly becomes acute in the affected areas. The pain is followed by marked pyrexia, at times associated with chills, and a sustained fever. Other constitutional symptoms are those of headache, anorexia, vomiting, and occasionally a depression of the central nervous system which may produce coma. In addition to the local pain there is a marked swelling of the limb with diffuse redness and pain in the regional lymph glands. The swelling, which is tender, is rather tense and does not pit. The duration of these attacks varies from two to eight days, occasionally lasting longer. Recovery, in contrast to the onset, is gradual; the temperature falls by lysis and the other manifestations become less prominent over a period of time. The above attacks have an acute onset and an irregular periodicity which is very characteristic. The onset occurs without warning and within a few hours the symptoms usually reach their maximum intensity. The intervals between attacks vary greatly; they may occur as frequently as once every week, but usually not more so than once a month and in many cases their recurrence may not take place more often than once in eight to twelve months. In the beginning these recurrences usually appear after longer intervals and, as the disease advances, these intervals become progressively shorter.

The clinical manifestations of elephantiasis are usually limited to the inconveniences caused by the extensive enlargement of the involved

Numerous workers, such as Allen and co-workers^{56, 57} Drinker,⁴²⁻⁴⁶ and others,⁵⁸⁻⁶⁰ have shown that in experimental and clinical lymphedema tissue fluids contain between 2.7 and 4.5 per cent protein. Drinker and his associates,⁴²⁻⁴⁶ experimenting with dogs, determined the protein content of plasma, lymph, and fistula fluid in a dog with elephantiasis. These were found to be 7.8, 5.5, and 4 Gm. per 100 c.c., respectively. This accumulation of protein favors the production of fibrous tissue, which results in fibromatosis in cases of elephantiasis. That such a mechanism undoubtedly operates in cases of lymph stasis with associated recurrent attacks of inflammation is suggested by this experimental work.

One should not dissociate the clinical features of the elephantoid condition from the progressive pathologic changes resulting from preceding acute attacks of lymphangitis and upon which the manifestations of the late stages depend. Matas^{1, 2} in 1911 and 1913 suggested that there are probably many factors capable of producing initial lymph stasis of both the inflammatory and noninflammatory types and that resulting edema, regardless of its mode of onset, increases the susceptibility of the involved area to infection by pyogenic organisms. He further states that once the inflammatory process has occurred the clinical picture and pathologic changes are identical, regardless of the initiating etiology. The acute inflammatory reaction is characterized by painful swelling of the infected area. This area becomes red and in many respects resembles the discoloration seen in erysipelas. However, the redness is more diffuse and seldom shows the blanching in the receding area behind the advancing red margin, as is characteristic in erysipelas. The regional lymph glands of the involved area become very much enlarged and tender. Numerous men report that in the extremities the acute reaction is seldom seen beyond the root of the limb. As this disease is primarily one of lymphangitis and not one of cellulitis, this observation can be explained on the anatomical arrangement of the lymphatics. Further extension of the process can only occur in the direction of the lymphatics, this being to the internal group of lymph nodes in the pelvis and aortic areas. However, it is conceivable that in rare cases the extension onto the lower abdomen from the thigh is possible by means of a retrograde flow of lymph. The tense lymphedema accompanying each attack of lymphangitis recedes somewhat as the disease subsides, but the size of the extremity never returns to that prior to the onset of the attacks. Consequently, the affected area becomes progressively larger with each attack and there is a permanent residual thickening of the subcutaneous tissues. This process is persistently progressive, eventually resulting in typical elephantiasis.

Histologic description, as given by various authors, has some minor differences as to the changes observed in cases of elephantiasis. Early descriptions, particularly those of Unna, emphasized changes in the venous system which consist of markedly dilated veins, possessing thick-

ened walls. Recently, attention has been focused on the alterations in the lymphatic system. Descriptions of these changes differ, some authors describing marked dilatation of lymph capillaries and smaller lymph vessels, others describing lymph soaked tissues in which they can find no evidence of existing lymphatic channels. Almost all authors agree that there are distinct areas showing coagulation of lymph within the lymph vessels. The changes occurring in the skin consist of a thinning of the epidermis with a thickening of the dermis. Occasionally a thickened epidermis showing hyperkeratosis has been described. The hair follicles disappear and the sweat glands show some degree of hypertrophy; collagen fibers of the subcutaneous tissues are swollen and are arranged in parallel bundles. The bundles, and in places the individual fibers, are widely separated by edema fluid. The overproduction of fibrous tissue replaces much of the adipose tissue and connects the skin with the thickened deep fascia. Elastic fibers, if present, are arranged in frayed bundles in which the individual fibers may be broken. Most authors state that there is a disappearance of elastic fibers. There is some disagreement as to changes observed in the blood vessels, but a thickening of the vascular wall is mentioned by many. The perivascular tissues show a slight round-cell infiltration.

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The clinical manifestations of elephantiasis are usually limited to the inconveniences caused by the extensive enlargement of the involved

area. In some instances this may be so extensive that complete loss of function is the result. The patient's complaints are almost entirely limited to those of inconvenience, plus a dull pain which is frequently associated with the increased weight of the involved extremity. In addition to the marked increase in size of the extremity the overlying skin is rough and coarse, having a *peau d'orange* appearance. At times the mouth of the hair follicles are gaping and the hair is usually very coarse. In the region of the ankle and knee the hypertrophied integument is thrown into heavy folds. Frequently, weeping ulcers with a surrounding eczematoid skin are present in the lower leg. In the region of chronic ulcers the skin is often pigmented and contracted, giving the appearance of an annular constriction.



Fig. 1.—X-ray of lower third of leg. A, Normal; B, elephantiasis.

In addition to the differences in the types of edema caused by other conditions due to systemic disease, including cardiorenal pathology, myxedema, etc., Reichert⁶¹ demonstrated the differences in x-ray findings of elephantiasis from the other edemas. He illustrated that in the advanced stage of lymphedema and elephantiasis there is a coarse trabeculation as well as marked thickening of the subcutaneous tissues. The muscle tissues and other deeper structures retain their relative normal size. These points are easily made out in soft tissue x-rays and are a diagnostic aid because in similar x-rays in other conditions with edema all of the tissues are usually involved. Our x-rays illus-

trate coarse trabeculation of subcutaneous tissue as described by Reichert.⁶¹ (Figs. 1, 2 and 3).

As suggested earlier, the successful treatment of this disease in all probability will depend upon a clear understanding of the etiologic factors and pathologic changes occurring during its course. Unfortunately, the patient seldom consults the physician during the initial attack or even early in the course of the disease. Even if the patient did consult the physician during the acute attack before the onset of characteristic fibromatosis, it is doubtful whether a diagnosis of pro-

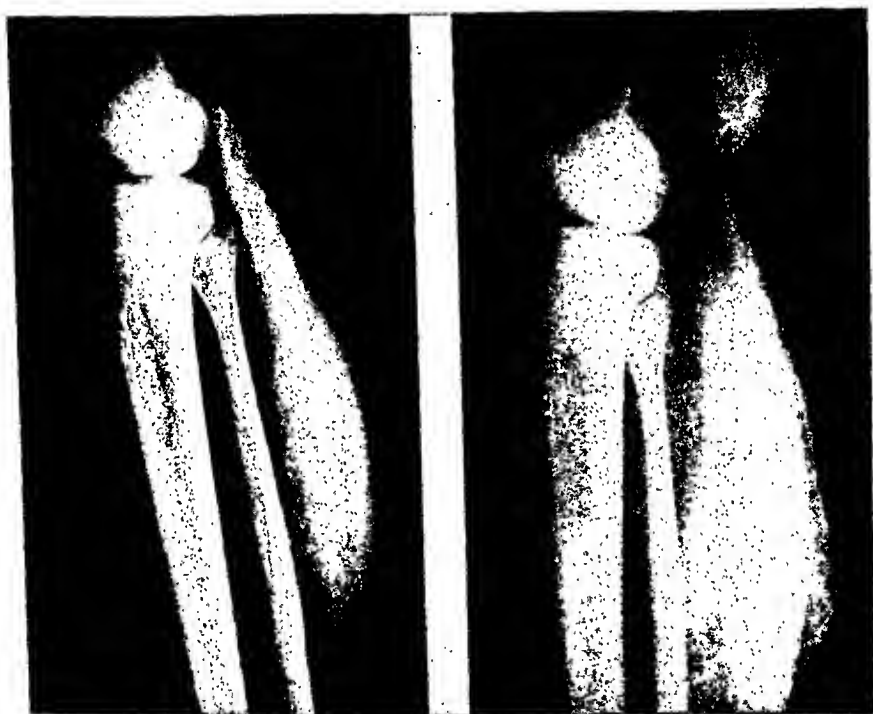


Fig. 2.—X-ray of upper third of leg. *A*, Normal; *B*, elephantiasis.

gressive lymphedema would be made; it is more likely that the patient would receive treatment for recurrent erysipelas. Prevention of recurrent attacks at this stage is the ideal form of therapy and every effort should be made to accomplish this. If this is successful, a great many surgical procedures will be obviated. Consequently, it should be constantly borne in mind that every case of lymphangitis is a potential case of progressive lymphedema and fibromatosis.

TREATMENT

As in the past, the therapy during the acute attacks of lymphangitis should be directed to the general systemic care of the patient plus the necessary measures to reduce local inflammatory reaction. Usually these will consist of bed rest, elevation of the extremity, and general

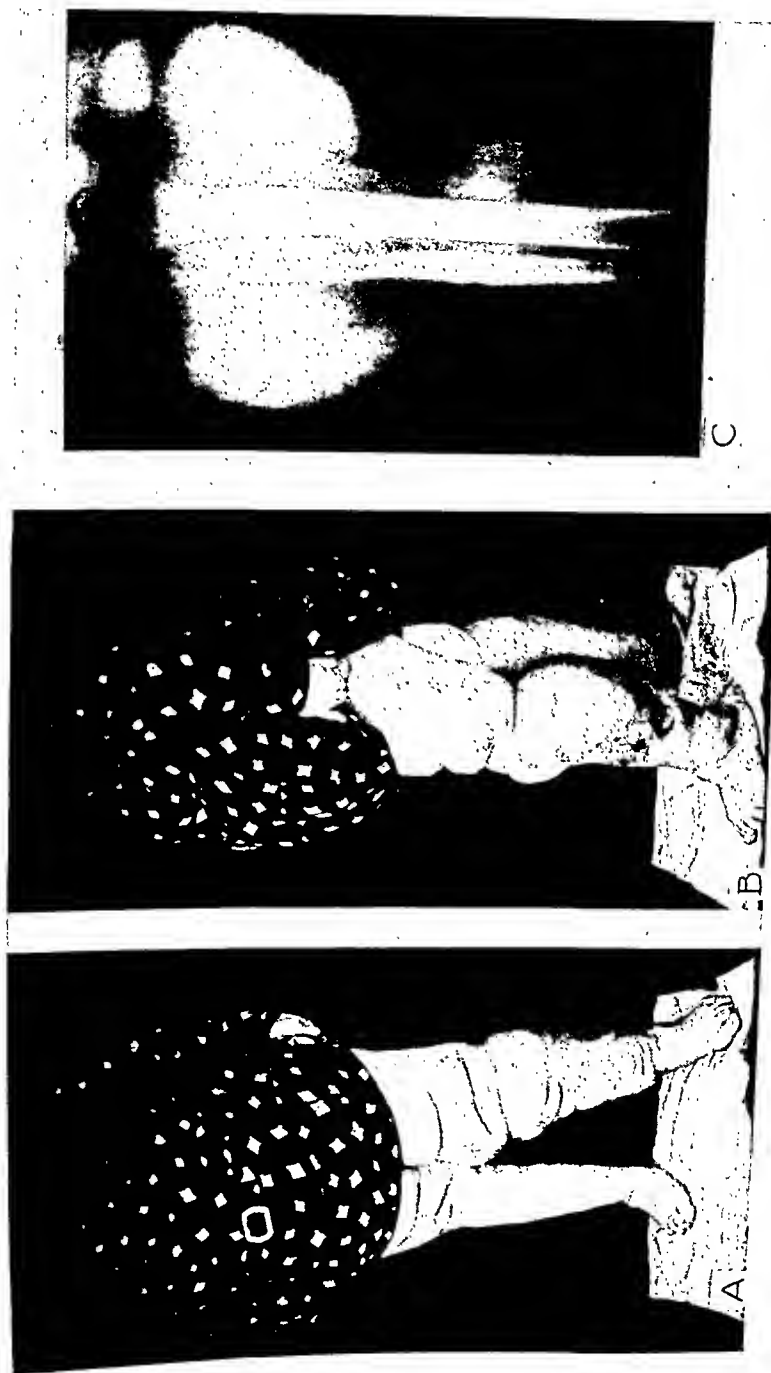


Fig. 3.—Photographs and x-ray of elephantiasis.

supportive measures. The value of vaccines and serum therapy is not questioned, but they have not proved to be of particular benefit in all cases. Beall,⁶² Flexner,⁶³ Gougerot and Blum,⁶⁴ Muller and Jordan,⁶⁵ Benson,⁶⁶ Memmesheimer,⁶⁷ and others have tried autogenous and polyvalent vaccines with success in many instances. Vaccines have shown a tendency in certain cases to decrease the frequency of recurrences. Symmers and associates,⁶⁸⁻⁷¹ Dick,¹² Birkhaug,⁷ Spink and Keefer,^{72, 73} Francis,¹⁷ Kolchin and co-workers,⁷⁴ and Spicer and co-workers,^{75, 76} and others⁷⁷⁻⁸⁵ found polyvalent streptococcic antiserum to be of great value in treatment of acute erysipelas, with good but not so striking results in recurrent cases. These same workers demonstrated that the use of polyvalent streptococcic antiserum does not modify in any way the frequency or the severity of recurrent attacks of erysipelas.

In addition to the specific therapy in recurrent acute lymphangitis it is important that the edema during the interval between acute attacks be prevented. The patient should keep the extremity bandaged with either an elastic stocking, rubber-roller bandage, or by some similar method; in addition baking and massage with periodic elevation of the extremity should be practiced. Exercise of the extremity when it is in the dependent position should be encouraged. These methods of controlling edema between recurrent attacks of lymphangitis could be instituted with benefit in those cases of chronic progressive edema in which there has been no history of an acute episode, because Drinker and his associates⁴²⁻⁴⁶ showed that lymph stasis predisposes to secondary infection. Also, there are numerous case histories of progressive lymphedema of many years' duration in which at no time has there been a flare-up of lymphangitis or other evidence of infection, which in later stages developed the manifestations seen in the type of lymphedema under discussion. Once this vicious cycle of infection and lymph stasis has occurred, its repetition is likely, as is the resulting elephantoid condition. Consequently, every case of progressive lymphedema, inflammatory or otherwise, should be treated with this in mind and every effort made to control further progression of the edema. The importance of preventing and controlling the edema cannot be too strongly stressed. Regardless of the etiology, edema predisposes to secondary infection. The inflammatory process resulting from the secondary infection produces a transudation rich in protein into the interstitial spaces which, due to the impaired lymphatic circulation, accumulates excessively. This protein plus the other products of inflammation is ideal for the production of fibrous tissue. It is because of this susceptibility of edematous tissue that the prevention of the edema is not only prophylaxis against infection, but, if completely controlled, may arrest the condition. This prevention of edema by suitable bandaging is most important and cannot be too strongly stressed.

Matas^{1, 2} first suggested that, because of the evidence favoring a streptococcal infection in this disease, an attempt should be made to immunize the patient against the streptococcus organisms. He advocated

the repeated injections of a polyvalent streptococcal antiserum over a long period of time. As evidence, he presented a patient who went through a course of repeated injections of 10 c.c. doses of antiserum, given at least three times a week. After sixteen injections the patient reported by letter from a distant city that this course of injections had given her considerable relief. However, she later reported that she had had a recurrence of lymphangitis. Matas^{1, 2} advised repeating the course of injections, but does not give the follow-up of this case. Since his original report, Matas has treated several patients with elephantiasis by repeated injections of antiserum. Although this treatment has not completely arrested the disease, he feels that it is of benefit in that it lengthens the interval between the attacks of acute lymphangitis and also lessens the severity of these attacks when they do occur. Apparently, this suggestion has not received a fair clinical trial in that there are no reports of its use. At Charity Hospital and the Hutchinson Memorial Clinic in New Orleans, Matas' suggestion was attempted in eleven cases, seven of which failed to complete the full course of immunization for various reasons beyond our control. The four remaining patients have received at least one complete course of injections of antiserum and in one instance a patient has received multiple series of injections. The patient receiving the multiple series of injections of antiserum and the one other who received only one course of treatment were not benefited by this form of therapy, both having recurrences without relief. The third patient, who has almost completed his first course of injections, experienced a recurrent attack shortly after starting the injections of antiserum. However, he has been free of symptoms during the last five months and feels that inasmuch as he was having recurrent attacks of lymphangitis about once a month he has been definitely benefited. In this case the indications are not only lengthening the interval between the attacks but are decreasing the severity of their manifestations. The fourth patient did not experience a recurrence during the course of treatment and has failed to return since its completion. Bertwistle and Gregg,⁸⁴ Pieard,⁸⁵ Elliott,⁸⁶ and Sézary and co-workers⁸⁷ advocate the use of antiserum in the treatment of this disease but fail to state that they have used it as outlined by Matas.^{1, 2} Consequently, clinical evidence is not sufficient to warrant conclusions as to the success or failure of this method of treatment. Although the accumulating evidence of a high degree of specificity in the strains of streptococci as related to their immune responses suggests that this method of therapy at times may fail, in some specific cases it is advantageous in preventing the recurrence of acute attacks of lymphangitis. A further clinical trial is indicated but it must be constantly kept in mind that the specificity of infecting organisms in certain cases may result in failure of response.

Without explaining the rationale, Low and Dixon,⁸⁸ McGolrick,⁸⁹ and others treated elephantiasis patients with intravenous injections of

nonspecific protein using T. A. B. vaccine. They fail to mention the nature of this vaccine, but report good results in the acute phase; however, their follow-ups are insufficient to warrant conclusions. There is one report of having used sulfanilamide⁹⁰ during the acute phase, but here again there is insufficient follow-up. In our experience sulfanilamide therapy in recurrent lymphangitis has been of no particular benefit in that it did not seem to alter the course of the acute attack or prevent recurrences.

The earliest reports of cases of elephantiasis were concerned primarily with the operative therapy. Of these, the reports of Lisfranc,⁹¹ who described a method of scarification of the tissues, and Carnochan,⁹² in 1851, who reported the ligation of the external iliac or femoral artery as a method of decreasing circulation and thus decreasing edema, were the first. Carnochan's⁹² procedure was used more frequently but many reported unsatisfactory results in that improvement did not follow and gangrene often developed. Handley,⁹³ in 1908, was the first to attempt to re-establish lymph circulation in lymphedema. His method consisted of placing silk threads parallel to the axis of the limb in the subcutaneous tissues. Various other modifications of this procedure have been advanced. Lexer⁹⁴ substituted strips of fascia for the threads, and Lanz,⁹⁵ in addition, trephined the femur and placed strips of the deep fascia into the trephined holes. Results of these procedures have been for the most part very disappointing. In 1912 Kondoleon⁹⁷ reported the procedure which bears his name. Ten Horn,⁹⁸ discussing operations used to establish increased lymph drainage, states that Payr, independent of Kondoleon, suggested a procedure similar to that described by Kondoleon. Consequently, this procedure probably should be called the Kondoleon-Payr operation. Kondoleon attempted to establish communication between the superficial and deep lymphatics by the excision of strips of deep fascia and placing subcutaneous tissues in contact with the muscle. Matas^{1, 2} was the first to perform a Kondoleon procedure in this country. His comments as to the efficacy of this operation were: "It is obvious that the possibilities of the new principle can only be tested by clinical experience and further observation. All that can be said of the observations thus far reported is that they are encouraging. It is with the hope that the simple procedure of Kondoleon⁹⁷ herein described may encourage others similarly placed to give a more extended and thorough trial to the method, that these early observations are recorded." Subsequent reports¹⁰⁰⁻¹¹⁸ indicate the operation met with indifferent success in the majority of cases. The lack of complete success resulted in various modifications by Sistrunk,¹¹⁹ Auchincloss,¹²⁰ Macey,¹²¹ and others;^{122, 123} however, all are based upon the same principle. These differ from the original Kondoleon⁹⁷ procedure in the following respects: the Sistrunk¹¹⁹ modification added the removal of overlying skin and a wedge of diseased subcutaneous tissue;

the repeated injections of a polyvalent streptococcic antiserum over a long period of time. As evidence, he presented a patient who went through a course of repeated injections of 10 c.c. doses of antiserum, given at least three times a week. After sixteen injections the patient reported by letter from a distant city that this course of injections had given her considerable relief. However, she later reported that she had had a recurrence of lymphangitis. Matas^{1, 2} advised repeating the course of injections, but does not give the follow-up of this case. Since his original report, Matas has treated several patients with elephantiasis by repeated injections of antiserum. Although this treatment has not completely arrested the disease, he feels that it is of benefit in that it lengthens the interval between the attacks of acute lymphangitis and also lessens the severity of these attacks when they do occur. Apparently, this suggestion has not received a fair clinical trial in that there are no reports of its use. At Charity Hospital and the Hutchinson Memorial Clinic in New Orleans, Matas' suggestion was attempted in eleven cases, seven of which failed to complete the full course of immunization for various reasons beyond our control. The four remaining patients have received at least one complete course of injections of antiserum and in one instance a patient has received multiple series of injections. The patient receiving the multiple series of injections of antiserum and the one other who received only one course of treatment were not benefited by this form of therapy, both having recurrences without relief. The third patient, who has almost completed his first course of injections, experienced a recurrent attack shortly after starting the injections of antiserum. However, he has been free of symptoms during the last five months and feels that inasmuch as he was having recurrent attacks of lymphangitis about once a month he has been definitely benefited. In this case the indications are not only lengthening the interval between the attacks but are decreasing the severity of their manifestations. The fourth patient did not experience a recurrence during the course of treatment and has failed to return since its completion. Bertwistle and Gregg,⁸⁴ Picard,⁸⁵ Elliott,⁸⁶ and Sézary and co-workers⁸⁷ advocate the use of antiserum in the treatment of this disease but fail to state that they have used it as outlined by Matas.^{1, 2} Consequently, clinical evidence is not sufficient to warrant conclusions as to the success or failure of this method of treatment. Although the accumulating evidence of a high degree of specificity in the strains of streptococci as related to their immune responses suggests that this method of therapy at times may fail, in some specific cases it is advantageous in preventing the recurrence of acute attacks of lymphangitis. A further clinical trial is indicated but it must be constantly kept in mind that the specificity of infecting organisms in certain cases may result in failure of response.

Without explaining the rationale, Low and Dixon,⁸⁸ McGolrick,⁸⁹ and others treated elephantiasis patients with intravenous injections of

have done sympathectomy the results have been disappointing, because as soon as the patient begins to walk after the sympathectomy there is an increase in the size of the extremity.

The majority of the recent operative procedures have been directed toward re-establishing a collateral lymph circulation, without taking into account the etiology of the production of the condition. In the literature there are numerous reports of workers^{100-118, 128-137} using these procedures and from them it is obvious that the only value of a surgical procedure is in the removal of considerable amount of tissue, thus decreasing the size of a limb. In so doing, in many instances there has been a partial return of function in a previously useless limb. However, in almost all of the cases there has been some, if not considerable, recurrence of edema as well as recurrence of acute lymphangitis. Most authors now feel that the only indication for operation is to remove or to restore the function of a limb, which, because of its size, is virtually useless. The operation is definitely contraindicated during the early stages of the disease.

Very few authors have commented upon the reasons for failure of the various operative procedures. An obvious explanation presents itself after a careful study of the anatomy of the lymphatic system, the infectious nature of the disease, and its pathogenesis. Keeping in mind the possible etiological factors involved, it is apparent that, with the exception of those operations removing considerable tissue, none of the surgical procedures are designed to attack the etiological factors which may be present. As suggested, such operations as the Sistrunk¹¹⁹ or the Auchincloss¹²⁰ modifications of the Kondoleon⁹⁷ procedure, or the recent operation of Macey¹²¹ in removing large areas of involved pathologic tissue might possibly at the same time remove the source of reinfection. This is in agreement with Unna's²² hypothesis that the disease is primarily one of streptococcal origin and recurrences result from persistence in the tissues of streptococcus in the dormant state during remissions. The recent work on the etiology of this disease has established the fact that in many instances the recurrences result from an entirely new exposure to the streptococcus. The portal of entry may be purely a local one, such as seen in cases resulting from local wounds, open ulcers, etc., or it may result from a more distant focus of infection, the local manifestations being explained by tissue sensitivity. A case illustrating this has been observed by one of us. This patient several years before the initial attack of erysipelas experienced a severe third degree burn of the right lower extremity which resulted in extensive cicatrization preventing the full extension of the knee. In succeeding years the patient's life was that of an active youth, participating in high school and college athletics. The activities with constant strain on the scar tissue resulted in a chronic recurring ulcer in the popliteal area. Approximately fourteen years after the injury, he experienced his first typical erysipelas attack which began above the malleolar area

Auchincloss¹²⁰ modified the Kondoleon-Sistrunk procedure by removing considerably more diseased subcutaneous tissue. In 1940, Macey¹²¹ reports his procedure of planting a full thickness graft on the deep fascia and resuturing the elephantoid skin over the graft. Two weeks later, the subcutaneous elephantoid tissue is excised and removed from over the graft. Preceding the report of Macey,¹²¹ Gillies and Fraser¹²³ outlined their plastic operation, which consists of bridging from the upper thigh to the abdomen by means of a flat pedicle graft of skin and subcutaneous tissues obtained from the arm. By this method, they attempted to establish communication between the lymphatics of the leg and those of the trunk.

Whereas blocking the sympathetic ganglia is of value in the treatment of edema associated with thrombophlebitis, both in the acute and in the chronic types, it is questionable whether it is of any value in cases of elephantiasis associated with recurrent erysipeloid infection. If, however, in a given case there is evidence of vasoconstriction either during the acute stage or subsequent to it, as can be determined by novocain block of the lumbar sympathetic ganglia, it is likely that the edema can be beneficially affected by interruption of the sympathetic impulses. Because, as previously reported by Ochsner and DeBaakey,¹²⁵ vasoconstriction associated with thrombophlebitis favors the production of edema and the relief of the vasoconstriction beneficially affects the accumulation of the fluid; the production of edema in vasoconstriction is probably due to the increased permeability of the capillaries, which in turn is caused by a relative anoxia resulting from the severe arteriolar spasm. Once the fluid which is rich in protein gets out of the vascular system into the perivascular spaces, it is difficult in cases with vasospasm for it to return to the vascular system, because the pump which is responsible for the movement of lymph, namely, arteriolar pulsation, is less effective. It has been shown by McMaster and Parsons³² and Cressman and Blalock³³ that arteriolar pulsations are largely responsible for the movement of lymph. By overcoming the vasospasm, the edema is beneficially affected, first by preventing the anoxia of the capillary endothelium and overcoming its increased permeability and preventing the excessive exudation of fluid into the perivascular spaces and also by favoring the movement of the lymphatic fluid by re-establishing the normal arteriolar pulsations. Jacquerye¹²⁶ reports nine cases of elephantiasis in which sympathectomy was done. All of these were improved with distinct diminution in the size of the extremity, disappearance of lesions and ulcers, and increase in temperature. However, the follow-up was not complete enough to warrant a final evaluation of the therapy. Basset, Haguenan, and Gauthron¹²⁷ performed a periarterial sympathectomy in a case of lymphedema without a satisfactory result. It is well known at the present time that periarterial sympathectomy is relatively ineffective in producing vasodilatation. Telford and Simmons⁴¹ state that in the cases of chronic lymphedema in which they

which these foci can be responsible for a recurrent lymphangitis. It is therefore obligatory for and the duty of the surgeon to search carefully for any possible focus of chronic infection in cases of progressive lymphedema. These may be found in local ulcers or fissures in associated epidermophytosis, chronic recurrent ulcers in scar tissue, and in the upper respiratory tract, including the paranasal sinuses, tonsils, teeth, and pharynx. It is important that these foci be eradicated as they may serve as ports of entry for streptococci.

SUMMARY

The role of secondary pyogenic infection, particularly that of streptococcus, in the production of recurrent attacks of acute lymphangitis resulting in elephantiasis is discussed. Elephantiasis is the end result of recurrent erysipeloid lymphangitis, produced by pyogenic infections, usually the streptococcus. Lymphedema is a predisposing factor for the pyogenic infection which causes the inflammatory reaction which is responsible for the ultimate fibromatosis.

Recurrent febrile attacks accompanying the erysipeloid lymphangitis are characteristic.

The treatment consists of prevention of the recurrent streptococcal infections and the avoidance of edema by the use of posture and compression bandages. Prolonged use of polyvalent streptococcic antiserum may be of value in some cases. Removal of foci of infection is of paramount importance.

Extirpation of diseased tissue is not justified until the infection has been eradicated. If appropriate conservative therapy is instituted early, surgical procedures usually can be avoided.

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and extending proximally involved the lower third of the leg. During the next four or five years, his attacks recurred at indefinite intervals, which became shortened as time progressed. During each attack the wide separation of the popliteal ulcer and the erysipelas infection was clear cut. Approximately six years after the onset and after innumerable recurrences of lymphangitis, a chronic recurrent ulcer in the popliteal area, as well as underlying scar tissue, was excised. A pedicle graft from the opposite thigh to the popliteal area was successful. Since this operation seven years ago, the patient has not experienced any further recurrences. It is obvious in this instance that stress upon the scar tissue in the popliteal area prevented the healing of the ulcer which, at a point some distance from the focus of infection, served as a portal of entry for the organisms responsible for the recurrent attacks of lymphangitis. Removal of this portal of entry resulted in a seven-year cure. Mulholland has similarly observed that in cases of recurrent lymphangitis of the erysipeloid type with epidermophytosis the dorsum of the foot is seldom involved, indicating a skip area between the toes and the erysipelous reaction. This being so, it is apparent that the operative procedure cannot offer more than temporary relief unless the source of the inciting factor is at the same time eradicated. In those cases which are a result of local infection, all local lesions should be carefully removed. In cases in which allergic phenomenon plays an important part, it is important not only to remove the foci of infection, but also to desensitize the involved area.

A review of the many etiological factors, as well as of the nature of the disease, which is primarily one of lymphangitis with secondary lymph stasis and edema, suggests that any operative procedure may be definitely harmful and is therefore contraindicated, if attempted before eradication of the inciting factors. If the source of infection persists after establishing collateral circulation of lymph, the recurrence of acute lymphangitis will only result in further extension of this inflammatory process into previously uninvolved channels. By so doing, deeper lymphatics are subjected to a pathologic process similar to that which produced the original condition. Therefore, an operation performed at this time not only opens new pathways for further extension of the disease, but at the same time by this extension of the disease tends to destroy the deep lymphatics and thus precludes the possibility of a successful operation at a later date, once the etiology has been controlled.

The importance of these foci of infection in causing the recurrence of lymphangitis in patients with progressive lymphedema cannot be overemphasized. Elliott⁴⁶ and MacKee¹³³ suggested that such foci could be important factors. Rhodes¹³⁹ also emphasized the importance of eradication of a focus of infection in the treatment of this disease. Stevens¹⁶ and others, in demonstrating the acquired sensitivity of previously infected tissues, have partially explained the mechanism by

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SURGERY

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No. 3

Original Communications

CHORDOMA

VICTOR RICHARDS, M.D., AND DON KING, M.D.,
SAN FRANCISCO, CALIF.

(From the Orthopedic Division, Stanford University School of Medicine)

HISTORY

SINCE Luschka¹ (1856) first directed attention to these rare tumors, which arise from remnants of the fetal notochord, more than 160 of them have been reported in the literature. The tumors which attracted his attention were small jellylike masses of tissue protruding intracranially from the base of the skull, apparently having arisen from the sloping surface between the sella turcica and foramen magnum (clivus blumenbachii).

Virchow,² a year later, attributed them to a degeneration of cartilage, and accordingly named them "eechondrosis physaliphora."^{*} In 1858 Muller³ suggested their origin from the notochord, which he was able to trace cephalad to the sella turcica. Klebs⁴ (1864) reported the first clinical case. It remained for Ribbert⁵ (1894), however, to establish their origin from notochordal tissue and to give them the name of chordomas. He punctured the intervertebral disks of rabbits and found that the resulting proliferation of the herniated nucleus pulposus closely resembled histologically that of chordoma. In 1910 Feldmann⁶ reported the first chordoma arising from the sacral region, and in 1919 Pototsehnig⁷ reported the first case with metastases. Many case reports have been submitted since, and excellent reviews of the cases can be found in the noteworthy articles of Stewart,⁸ who presented 26 cases in 1922; Coenen,⁹ 68 cases in 1925; Stewart and Morin,¹⁰ histologic criteria for diagnosis in 1926; Machulko-Horbatzewitsch and Roehlin,¹¹ review of 35 cases of sacrococcygeal chordomas in 1930, 103 cases in all; Owen, Hershey, and Gurdjian,¹² review of 9 cervical cases in 1932; Fletcher, Woltman, and Adson,¹³ review of 75 cases of sacrococcygeal chordomas

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*Eechondrosis means from cartilage; physaliphora, vacuole-containing cell.

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of the second and third lumbar vertebrae. The left thigh was distinctly smaller than the right; the muscle groups of both thighs were weak, but no palsies existed. No sensory changes could be detected. Both knee and ankle jerks were absent, but no pathologic reflexes were noted. Proprioception was normal; vibration sense was bilaterally diminished. The left abdominal reflexes were greatly diminished; the rectal sphincter tone was good.

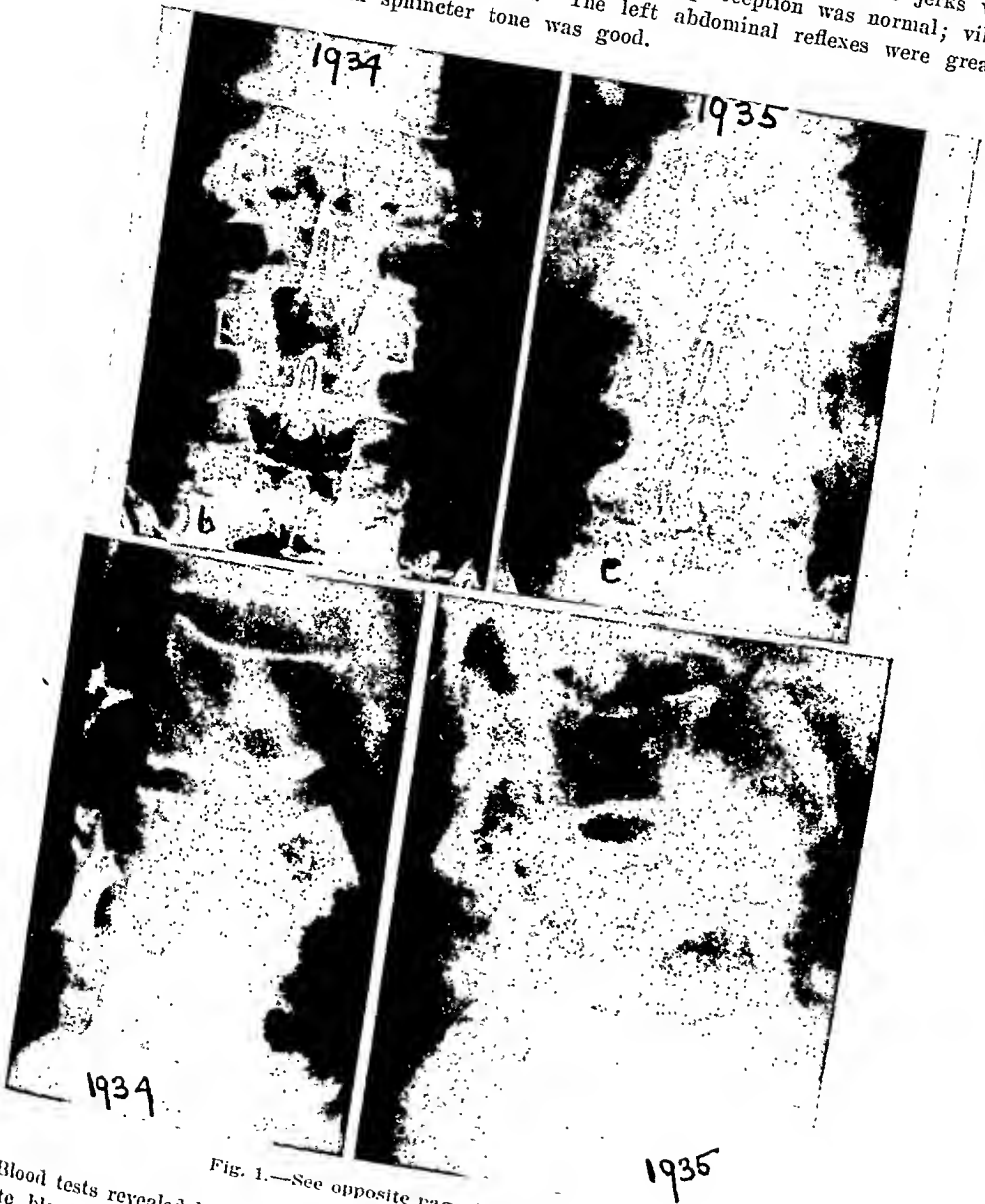


Fig. 1.—See opposite page for legend.

Blood tests revealed hemoglobin, 72 per cent (Sahli); red blood count 3,660,000; white blood count, 9,600, with normal distribution. Routine urine studies were negative; no Bence-Jones protein was found. The Wassermann test was negative; the stool was negative. The erythrocyte sedimentation rate was 11 mm. per hour (Wintrobe). The results of x-ray examination are shown in Fig. 1.

in 1935; and Mabrey,¹⁴ comprehensive study of 150 cases of chordoma in 1935. About 20 cases have been reported since 1935, enlarging the scope of the subject and emphasizing various unusual features.

During the past two years we have observed a patient with a large chordoma, apparently arising from the third lumbar vertebra. A review of the case history is given below.

CASE HISTORY

Mr. O. J., 52-year-old white American, a bookkeeper, entered the Stanford-Lane Hospital on Sept. 14, 1937, complaining of lumbar back pain of five years' duration. The family and past histories threw no light upon the present illness, which began early in 1932 with the appearance of sharp pain in the lumbar back, radiating to the buttocks and upper thighs. X-rays a short time later (Fig. 1a) were



Fig. 1.—Serial x-rays of lumbar spine in years indicated.

negative. At first these pains occurred approximately every two months, but they gradually increased in frequency and severity so that by May, 1934, a diagnosis of spinal cord tumor was made. Since then he had been treated with maximum x-ray therapy, casts and braces. The pain was somewhat relieved, but his legs had become progressively weaker with a concomitant feeling of numbness in the thighs, leading to complete inability to walk in the few weeks prior to entry here. During the past few months he had noticed increasing constipation and nocturia one to two times a night, and three weeks ago a firm mass appeared in the right upper quadrant. He had lost 40 pounds in weight in the past two years.

Examination.—The patient looked generally thin and sallow and showed evidence of moderate weight loss. The temperature, pulse, and blood pressure were normal. The abdomen was slightly distended, and the soft edge of the liver was just palpable at the right costal margin. The entire right upper quadrant was occupied by an immense, deeply placed, stony hard mass which was immobile, nontender, and apparently retroperitoneal in origin. No other masses were detected, and generalized lymphadenopathy was absent. A striking deformity was present in the spine, which had a right lumbar scoliosis and a projecting kyphosis in the region

"The tumor shows a honeycombed structure, the latticework of which is composed of notochordal cells surrounded by tiny lacunae. The interstices of the lattice framework contain a homogeneous mucinlike material. No mitotic figures. This histological picture is typical of chordoma." (Fig. 2.)

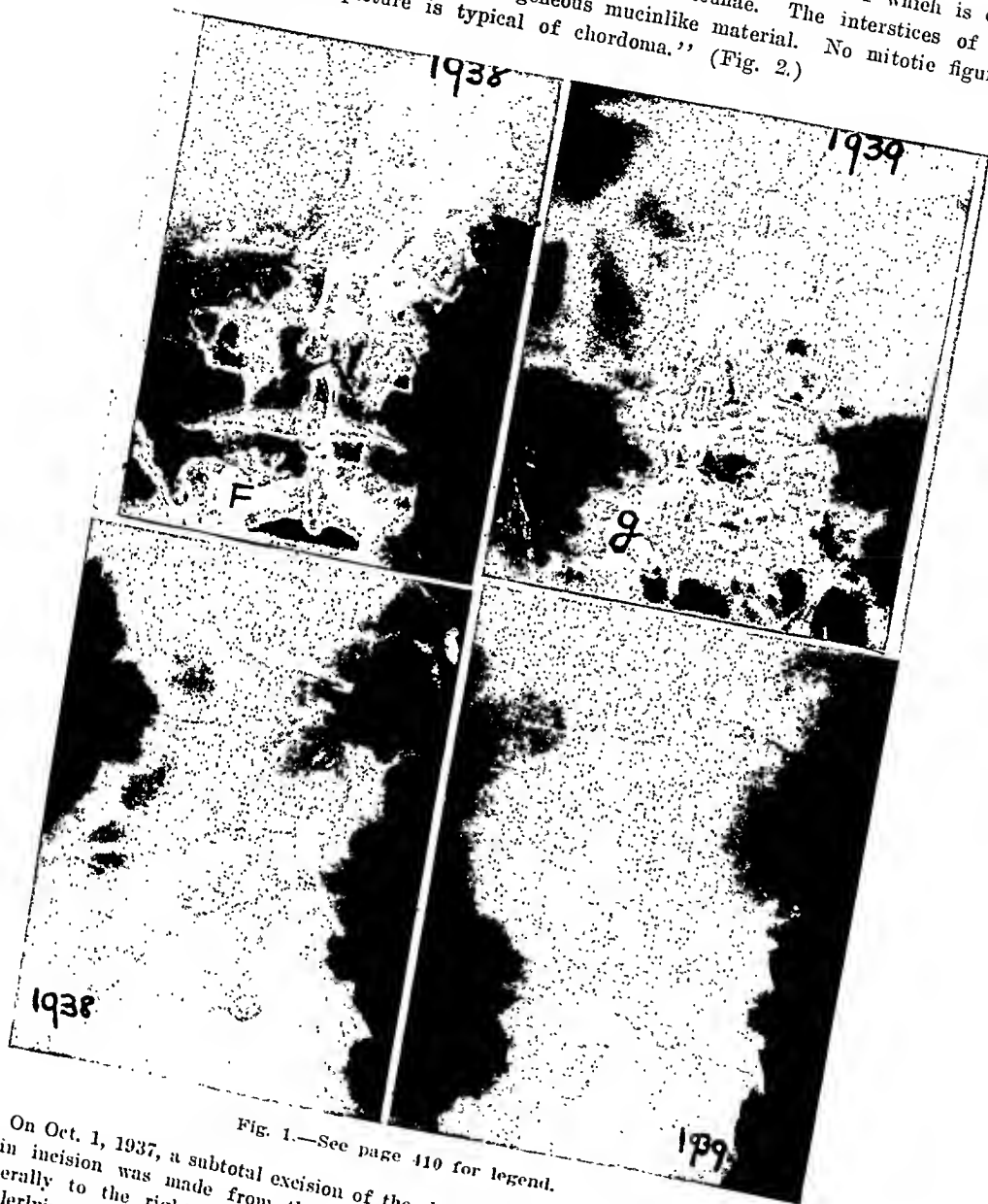


Fig. 1.—See page 410 for legend.

On Oct. 1, 1937, a subtotal excision of the chordoma was effected. A longitudinal skin incision was made from the first lumbar vertebra to the sacrum, curving laterally to the right in order to avoid the area of roentgen erythema. The underlying fascia was divided in the line of the skin incision and reflected medially. Bleeders were caught and coagulated with the high frequency current. The lumbosacral and erector spinae muscles were separated from the right side of the spinous processes, divided transversely at the level of the third lumbar vertebra

The entire third vertebral body and its transverse processes on the right were destroyed. Only a little of the second vertebral body remained. The twelfth thoracic vertebra was greatly compressed, and also the first lumbar was somewhat compressed. The fourth lumbar vertebra was partly destroyed. An irregular zigzag streak of density seemed to arise from behind the crests of the right ilium. It wandered upward to the region of the third lumbar vertebra. This might be connected with the mass palpable on physical examination. The ribs were normal. The radiologists felt the picture was probably that of metastatic carcinoma.

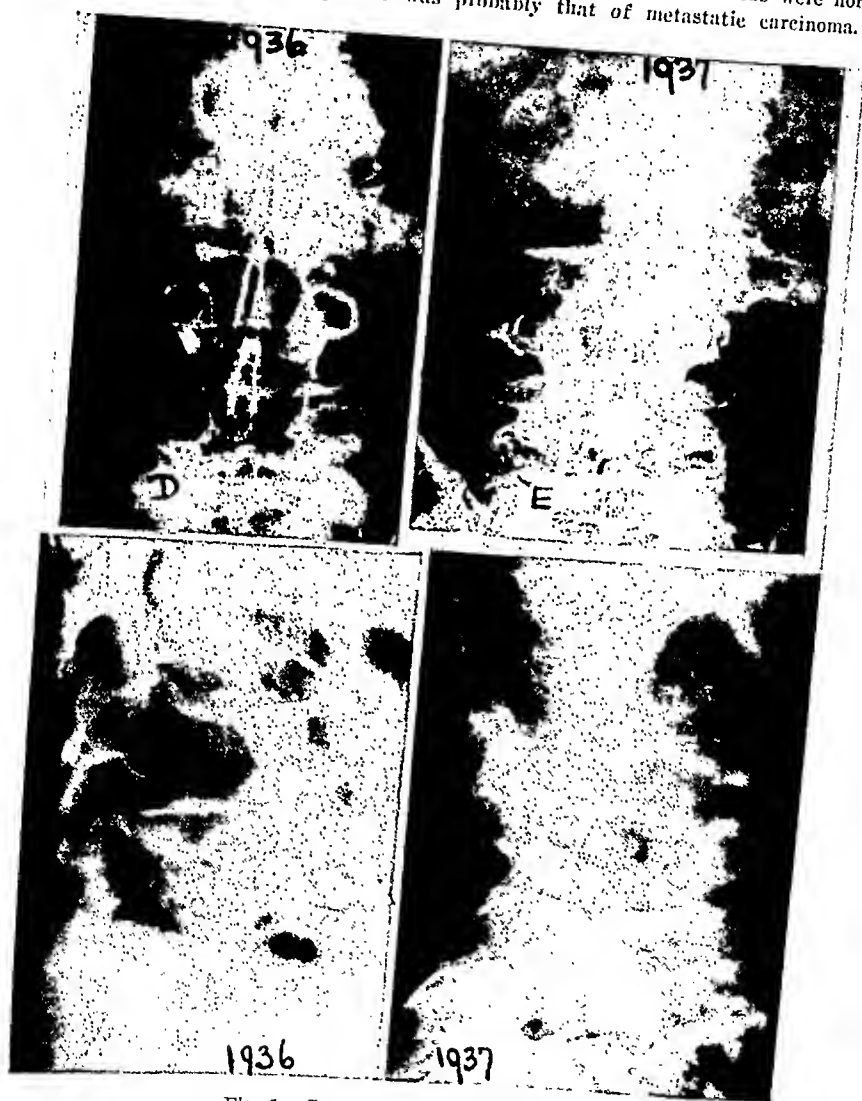


Fig. 1.—See page 410 for legend.

The conclusion from intravenous urograms was "an extrarenal tumor displacing the right kidney upward and outward."

An aspiration biopsy was taken from the spinal mass on Sept. 25, 1937. The pathologic report was as follows:

absolute alcohol was injected into the fourth and fifth lumbar vertebrae just to the left of the cord, without relief of symptoms. He was dismissed on Nov. 13, 1937, without much improvement. There was a draining sinus at his operative site.

On Jan. 7, 1938, he re-entered the hospital. In the interim he had been confined to bed. The sinus continued to drain, and the leg weakness persisted. The leg pain was dull, aching, and particularly severe on the left, necessitating opiates for relief. No new symptoms had appeared, and he still had control over his bladder and bowels.

Examination on this entry showed marked atrophy of both lower legs, especially of the quadriceps group on the left, absent deep reflexes bilaterally, no pathologic reflexes, diminished proprioception, especially on the left, and losses of epicritic sensation on the left without relation to the cord segment distribution. Checkup x-rays showed an increase in the destructive process involving the patient's lumbar spine (Fig. 1f). The right half of the third lumbar vertebra had almost completely disappeared, and only a thin shell remained on the opposite side. The left transverse process remained; the other vertebrae adjacent to this site show some increase in bone condensation, and this is probably the result of x-ray therapy. As a result of the disease process, the second and fourth lumbar vertebrae approach each other, obliterating the third lumbar intervertebral space. The fourth and fifth lumbar vertebrae have slipped forward a few millimeters.

The patient was placed in a body cast which was bivalved and to which buckles were applied. He was dismissed on Jan. 16, 1938, wearing the body cast while upright, and removing it when lying down. He felt quite well and was encouraged by his condition.

Mr. O. J. was next seen on July 16, 1939. In the intervening nineteen months he had been completely bedridden. Very little change had occurred in his symptomatology or the outcome of physical examination. The pains in the legs persisted and were, if anything, a little less than before. This pain necessitated from 2 to 3 gr. of morphia daily. He had retained control over his bladder and bowels. There was marked atrophy of both lower extremities. The only paralysis present was that of the left quadriceps group. No anesthesia was present, either in the sacrum or in the lower extremities. The operative incision was well healed. The tumor had increased tremendously in size. The entire lumbar region was filled with a large, irregular, lobulated mass about 10 by 20 cm. in size. It extended up onto the right lower ribs, and downward into the sacrococcygeal region which also was distorted by a roughly circular, midline, 10 cm. mass with exuberant fungation and ulceration in its central 5 cm. The liver and spleen were not palpable. Deep in the right lower quadrant a large, irregular, nodular mass could be detected, corresponding to the visible external tumor.

No clinical evidence of metastases could be discerned, and a complete skeletal survey demonstrated only a generalized osteoporosis undoubtedly due to prolonged bed rest (Fig. 1g).

EMBRYOLOGY

Within the second week of embryonic life a groove appears on its long axis. The lateral walls of this groove expand dorsal and medialward to coalesce, thus forming the neural tube (Fig. 4). Just under this canal the archenteric endoderm arches upward and becomes pinched off to form another tube, the notochordal canal. Later the lumen of this canal disappears, so that a solid cord of cells lies between the neural tube and the archenteron, extending throughout the entire

with a radio-knife, and retracted. The larger portion of the tumor was thereby exposed. It was, roughly, 8 cm. in diameter, well-encapsulated, and extended not only upward into the erector spinae muscles, but also had eroded the laminae of the second and third lumbar vertebrae. The tumor was mobilized extracapsularly as much as possible by careful dissection. However, complete mobilization was not feasible, for, on reflecting the tumor to the right, the dura of the second and third lumbar vertebrae was found exposed, the nerve roots of the second and third lumbar vertebrae traversed the tumor, and a large portion of the tumor extended anterior to the vertebral bodies. Accordingly, the capsule of the tumor was incised, and the soft, jellylike, grossly nodular and trabeculated, grayish-red tumor was removed piecemeal with a uterine curette. When as much as possible of the tumor had been removed, the wound was closed in layers, catgut being used throughout.



Fig. 2.—Microscopic section showing characteristic vacuolated, mucin-containing cells, extracellular mucus, and lobular arrangement of the tumor cells.

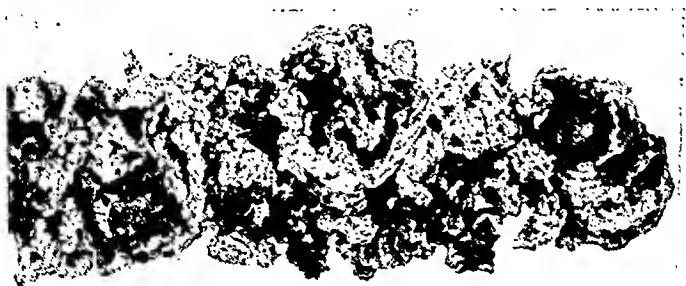


Fig. 3.—Gross specimen of tumor.

Postoperatively the patient ran a rather stormy course. The wound became infected with *Bacillus coli* and *B. welchii*. It drained considerably, but under treatment with Dakin's solution it gradually decreased in size and granulated in. Symptomatically he was only slightly benefited. On November 11, 0.8 c.c. of

below. The body of each vertebra necessarily contains the embryonic notochord (Fig. 6). In the adult traces of the notochord can be found only in the nucleus pulposus in the intervertebral discs. The pedicles and lamina of the vertebrae are formed by dorsal extensions of the body over the neural tube. The various ligaments of the vertebral column differentiate from the mesenchyme surrounding the vertebrae.

Theory of Resegmentation after Remak and Bardean
Schematic Diagram of Vertebral Development

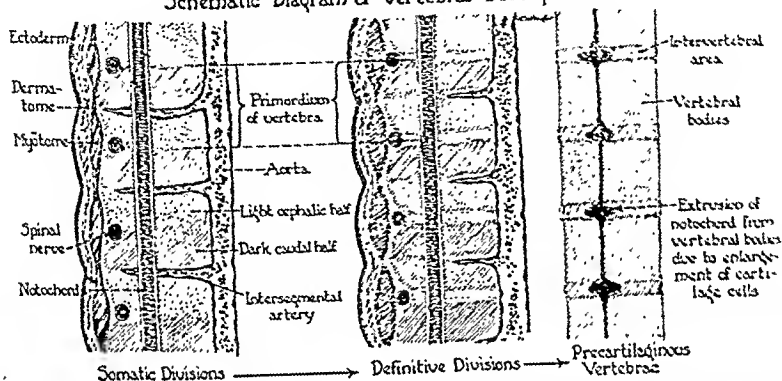


Fig. 6. (From Keyes and Compere: J. Bone & Joint Surg. 30: 898, 1932.)



Fig. 7.—Recent photograph of the patient (July, 1939). Rounded masses of tumor are visible in the right back and loin, protruding under the skin. The operative scar is visible. There is an ulcer over the sacrum from a pressure sore, and the dressing posterior to the right great trochanter covers a pressure sore.

It is of particular interest, in view of the origin of some chordomas from the dens of the epistropheus, to review the embryologic development of the atlas and axis. When the atlas is forming, its body fuses with that of the axis and becomes the dens of the latter, leaving the atlas shaped like a ring. The embryonic notochord, therefore, runs right

length of the future vertebral canal from the tip of the tail to the dorsum sellae of the sphenoid bone (Fig. 5).

From the mesoderm surrounding the neural tube and notochord, the skull, vertebral column, and membranes of the brain and spinal cord are developed. The sclerotomic mesenchyme comes to lie in paired

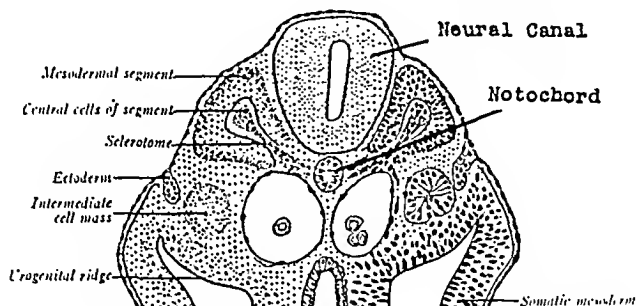


Fig. 4.—Transverse section of a 4.5 mm. human embryo. (Kollmann)

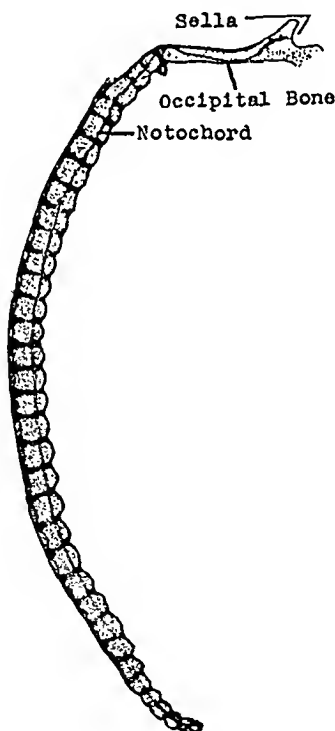


Fig. 5.—Drawing showing extent of embryonic notochord. (Williams: *Am. J. Anat.* 8: 251, 1908)

segmental masses alongside the notochord. Each sclerotomal segment divides into two segments, a caudal dense half, and a looser cranial half. The vertebrae are formed by the fusion of the denser caudal half of each sclerotome above, with the looser cranial half of the sclerotome

Some of the larger tumors involved two regions. Attachment to the bone was the rule, but not a constant finding, and bone destruction is characteristic.

TABLE II
MABREY (1935)

| | | | |
|-----------------|----|---|-----------|
| CRANIAL: | | | |
| Clivus | 29 | } | 49 |
| Occipital bone | 2 | | |
| Hypophyseal | 6 | | |
| Nasopharyngeal | 10 | | |
| Alveolar | 2 | | |
| VERTEBRAL: | | | |
| Cervical | 7 | } | 14 |
| Thoracic | 2 | | |
| Lumbar | 5 | | |
| SACROCOCCYGEAL: | | | |
| Antesacral | 41 | } | 87 |
| Retrosacral | 29 | | |
| Central | 17 | | |
| | | | <hr/> 150 |

GROSS PATHOLOGY

Two gross types of pathology are worthy of separate consideration: (1) the *ecchondrosis physaliphora*, and (2) the true chordomas.

Ecchondrosis Physaliphora.—These are small, soft, jellylike non-neoplastic masses attached by a pedicle to the dorsum sellae. Since they are asymptomatic and have been reported as an autopsy finding (Ribbert, 2 per cent), they have no clinical significance.

Chordomas.—These are truly neoplastic. The consistency varies, but they are usually soft, jellylike, translucent, and milky-white, grayish, or pink in color, depending upon the vascularity and the amount of hemorrhage. The surface is smooth, but gross nodularity is present. They are well encapsulated, and the cut surface shows fibrous trabeculae producing the gross nodularity and lobulation. Each lobule is semi-transparent, grayish to red, depending upon the vascularity and hemorrhagic foci. The more mucinous the character of the tumor, the more benign it is. The malignant ones are opaque, with little mucin.

Less common features are large amounts of cheesy necrosis and jellylike cystic masses.

The cranial chordomas may grow up intracranially or down into the nasopharynx through the craniopharyngeal foramina. Bone destruction is usually present. The sacrococcygeal chordomas may invade the pelvic muscles or the rectum, thereby simulating very closely rectal colloid carcinoma. They are usually locally destructive and recurring. Widespread metastases are not infrequent in the sacrococcygeal group (over 50 per cent). Metastasis to the dorsal spine has been reported from one case of intracranial chordoma.

through the dens and the apical odontoid ligament to reach the base of the occipital bone.

The sacral and coccygeal vertebrae represent types with reduced vertebral arches, and, consequently, the notochordal remains lie in their centers.

Some notochordal cells must of necessity remain in the centers of the vertebral bodies.

ANATOMIC LOCATION

Chordomas are true neoplasms of the notochord. Some believe these tumors arise from the nucleus pulposus, while others maintain as strongly that their origin is from the chordal rests within the bodies of the vertebrae, or from isolated aberrant foci of chordal cells on the anterior or posterior surfaces of the vertebrae. Anatomically, the tumor seems to arise within, or adjacent to, the vertebral bodies, and not from the intervertebral discs. Not infrequently the tumors are not attached to the spine, although bone destruction is an almost constant finding.

CLASSIFICATION AND DISTRIBUTION

Chordomas may arise anywhere in the course of the notochord, but they are most frequently found at the sphenooccipital and sacrococcygeal regions. In the 103 cases of Machulko-Horbatzewitsch and Rochlin (Table I) the cranial and caudal cases were of approximately equal

TABLE I
MACHULKO-HORBATZEWITSCH AND ROCHLIN (1929)

| | | | |
|----------------------------|----|--|-----|
| CRANIAL: | | | |
| Clivus | | | |
| benign | 21 | | |
| malignant | 18 | | |
| Hypophyseal | 1 | | |
| Nasopharyngeal | 5 | | 49 |
| Dens | 1 | | |
| Jaw | 2 | | |
| Occipital | 1 | | |
| VERTEBRAL: | | | |
| Cervical, thoracic, lumbar | 8 | | 8 |
| CAUDAL: | | | |
| Central | 4 | | |
| Peripheral | 42 | | 46 |
| retrosacral | 8 | | |
| antesacral | 34 | | |
| bony | 32 | | |
| intestinal | 2 | | |
| | | | 103 |

occurrence; in the later series of 150 cases by Mabrey (Table II), sacrococcygeal tumors occurred twice as frequently as those of the sphenooccipital region. These two classifications are shown in Table II.

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The tumors may reach an enormous size, the largest one reported being 20 by 30 cm.

HISTOLOGY

Early in the history of chordomas these tumors were confused histologically with colloid carcinomas, mucoid or signet ring carcinomas, myeloblastomas, chondromas, and spindle-cell sarcomas. The histology is, however, specific.

The essential histologic features are: (1) intra- and extracellular mucus; (2) vacuolization of the cellular elements; and (3) lobular arrangements of the tumor cells which usually grow in cords (Fig. 2).

Microscopically, the tumor is seen to be composed of islands of parenchyme separated by strands of connective tissue. Many of the islands are richly cellular, consisting of closely packed cells of an epithelial type. The cells of some of the lobules, however, are vacuolated due to the presence in their cytoplasm, and not infrequently in their nuclei, of mucin. The amount of mucin contained in the cells varies considerably, and hence, then, the marked variation in their size and shape. Extracellular collections of mucus are also visible to a varying extent, some lobules consisting almost entirely of this structureless material.

AGE AND SEX INCIDENCE

Age.—Chordomas have been found in all age groups from a 7-month fetus to an 82-year-old person. The majority of the sphenoccipital chordomas are recognized between the third and fourth decades, while most of the sacrococcygeal chordomas have occurred between the fifth and sixth decades. The average age occurrence of 150 cases of Mabrey was:

| | MALES | FEMALES |
|----------------|-------|---------|
| Sphenoccipital | 40 | 40 |
| Sacrococcygeal | 50.5 | 43.2 |

The average duration of symptoms before seeking medical advice in the two groups was approximately thirty-eight months each. The delayed appearance of chordomas is unexplained.

Sex.—*

| | SACROCOCYGEAL | SPHENOCCIPITAL | TOTAL |
|------------|---------------|----------------|-------|
| Males | 58 | 26 | 84 |
| Females | 27 | 17 | 44 |
| Not stated | 1 | 3 | 4 |
| | 86 | 46 | 132 |

Sphenoccipital chordomas occur with approximately equal frequency in both sexes; sacrococcygeal chordomas occur roughly twice as frequently in the male as the female, suggesting the possible role of trauma.

*Table from Mabrey.

SYMPTOMS

General.—The symptomatology varies with the region affected and is the direct result of mechanical pressure.

Cranial Chordomas.—The most common clinical symptoms of intracranial chordomas are pain, visual disturbances, multiple nerve palsies, dizziness, tinnitus, speech difficulty, and the symptoms of intracranial pressure—headache, nausea, and vomiting. Choked disks are not frequent, and pituitary disorders are rare considering the location of these tumors. The tumor usually remains within the cranium, but not uncommonly it may grow into the nasopharynx, producing difficulty in breathing.

Cervical Chordomas.—About twelve to fourteen cases of cervical chordoma have been reported, these tumors arising from the dens, intervertebral disks, or vertebral bodies. They grow in the pharynx or into the lateral aspects of the neck, producing spinal cord pressure with radicular pains, palsies, and muscle atrophies. All cases reported were diagnosed preoperatively as tuberculosis of the cervical spine.

Thoracic and Lumbar Chordomas.—These chordomas produce symptoms of localized bone involvement and evidences of spinal cord compression. Nothing diagnostic is present. Tuberculosis or metastatic neoplasm is the usual clinical diagnosis before biopsy. The spinal fluid may be xanthochromic.

Sacrococcygeal Chordomas.—Pain is the most common symptom, and its type and severity vary from a dull ache to sciatica or radicular pains, depending upon the relation of the tumor to the spinal cord and nerve roots. Pain antedates the visible external mass in about 50 per cent of the cases. The tumor mass is almost invariably found either by palpation of the sacrococcygeal region or by rectal examination. Skin ulceration is uncommon. The antesacral type may invade the perineal tissues, leading to genitourinary difficulties, such as dysuria, frequency, burning, urgency, nocturia, and dribbling; or the rectum, resulting in constipation, rectal tumor, hemorrhoids, rectal bleeding, sphincteric disorders, and, occasionally, ulceration of the rectal mucosa. Symptoms of cord pressure are also evident, and in this group metastases may be present.

DIAGNOSIS

The differential diagnosis includes: intracranial neoplasms, vertebral tuberculosis, metastatic neoplasm, giant-cell tumor, hemangioma, colloid carcinoma of the rectum, osteoma, chondroma, and chondrosarcoma.

The history and the clinical and x-ray examinations are not pathognomonic. Biopsy is necessary to positive diagnosis, and the consistency of the tumor permits biopsy by aspiration.

PROGNOSIS

Cranial.—The average duration of the disease from the onset of symptoms is from twenty-nine (Mabrey) to thirty-four months (Stewart and Morin). Some patients have died in four months; the longest case reported was that of a patient who had symptoms for over eighteen years prior to death.

Vertebral.—The average length of life after onset of symptoms was seventeen and one-half months.

Sacrococcygeal.—The average duration of life after the onset of symptoms was from six and one-half to seven and one-half years.

| | DURATION OF LIFE FROM ONSET OF SYMPTOMS |
|----------------|--|
| Cranial | 2½ to 3½ years |
| Vertebral | 1½ to 2 years |
| Sacrococcygeal | 6½ to 7½ years |

TREATMENT

The best form of treatment is local excision of the tumor as a palliative measure, combined with maximum doses of high voltage x-ray. Rarely can complete excision of the tumor be effected. Local recurrence is the rule, usually in from seventeen to twenty months. The operative mortality in fifty-nine cases in Mabrey's series was about 30 per cent. The best surgery offers is the alleviation of pain, retardation of the growth, and control of neurologic symptoms. Irradiation alone offers less. Rare cases of complete surgical cure have been reported.

SUMMARY

The history, origin, pathology, and clinical facts regarding chordomas are reviewed. An interesting case of this rare tumor is presented. The progressive and extensive bone destruction produced by this tumor is well shown in the series of x-ray studies. Its consistency permits biopsy by aspiration. The amount of nerve involvement is minimal for the size and location of the tumor.

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VARIATIONS IN ORIGIN AND COURSE OF THE HEPATIC ARTERY AND ITS BRANCHES

IMPORTANCE FROM SURGICAL VIEWPOINT

E. ZOLLICOFFER BROWNE, B.A., M.D., NEW ORLEANS, LA.

(From the Department of Gross Anatomy, Tulane University Medical School)

IN 1935, after dissecting the root structures in 60 cadavers, I wrote an article on the right hepatic artery.¹ Since that time, the study of dissected specimens has been continued until the total of 280 has been reached, a series which is used as a basis for the present article on the entire hepatic artery.

This large number (the largest yet used in medical literature) should give a fair representation of what to expect in actual practice, for the general rule is always applicable that the larger the sample the more reliable are the conclusions that may be drawn regarding the entire human race.

This article will be a study in both anatomy and surgery, as it properly should be, for is not surgery, in the most part, really applied anatomy.

DEFINITION OF TERMS

The term, common hepatic artery, denotes the hepatic artery from the origin of this vessel until it divides into its terminal right and left branches. It should be realized, however, that some textbooks consider the common hepatic as stopping when the artery enters the gastrohepatic omentum and call the trunk running in the omentum by the name of hepatic proper (or propria).

By the term normal common hepatic is meant an artery arising from the celiac axis and supplying both lobes of the liver.

By replacing common hepatic is meant a hepatic artery, supplying both lobes of the liver, but arising from another source than the celiac axis.

By accessory common hepatic is meant an additional hepatic artery (one or more) supplying both lobes of the liver in addition to a normal common hepatic. The origin of this accessory branch may also be from the celiac.

By absence of the common hepatic is meant that the right and left lobes are supplied separately by separate arteries. In this case the artery to the right lobe would be a replacing right hepatic and the one to the left lobe a replacing left hepatic. No common hepatic trunk is present.

The terms normal, replacing, accessory, and absent are also used in the discussion of the branches of the common hepatic artery, wherever their use is feasible.

By common hepatic duct is meant the extrahepatic bile passage from the union of the right and left hepatic ducts to the point of union with the cystic duct. The ductus choledochus (common bile duct) extends from this point to the ampulla of Vater in the descending portion of the duodenum.

The use of other terms and extent of structures referred to will be readily apparent.

COMMON HEPATIC ARTERY

A. *Normal*.—In the present series of 280 cases the common hepatic originates in a normal way in 260 cases (92.8 per cent). This number compares with the series of other investigators as shown in Table I.

TABLE I

| AUTHOR | CASES EXAMINED | FREQUENCY | PERCENTAGE |
|-----------------------------------|----------------|-----------|------------|
| Adachi ² | 252 | 224 | 83.3 |
| Brewer ³ | 50 | 46 | 92.0 |
| Branco ⁴ | 50 | 46 | 92.0 |
| Descomps ⁵ | 50 | 50 | 100.0 |
| Kosinski ⁶ | 55 | 48 | 87.0 |
| Leriche and Villemin ⁷ | 55 | 52 | 94.5 |
| Lipschutz ⁸ | 83 | 70 | 84.3 |
| Rossi and Cova ⁹ | 102 | 92 | 90.2 |
| Susloff ¹⁰ | 131 | 125 | 95.4 |
| Thompson ¹¹ | 50 | 44 | 88.0 |
| Browne | 280 | 260 | 92.8 |

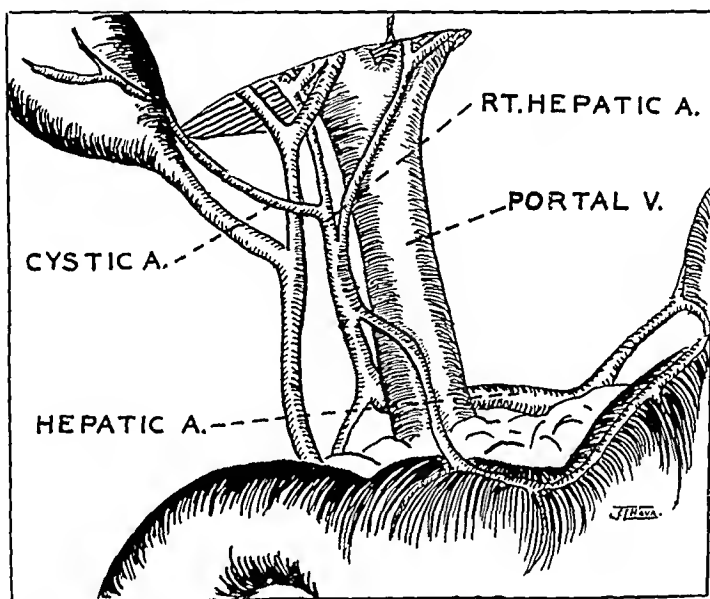
Two hundred and two of these arteries had long trunks and divided into right and left terminal branches about 1.5 cm. from the porta hepatis. These are the so-called classic type vessels of Branco.⁴ The other 58 had short trunks and divided into terminal branches at the point where the gastroduodenal branch is given off. These short vessels are the so-called *en bouquet* type of Branco,⁴ as they appear to terminate in a bunch. Some authors class this as low bifurcation of the vessel, but it is really a trifurcation, composed of the two right and left branches and the gastroduodenal branch.

Ten of the trunks of the long (classic) type had abnormal courses, sufficient to warrant special description. One passed posterior to the portal vein (Specimen 88, Fig. 1). This seems to be a very *unusual* relationship for a common hepatic (celiac origin). Branco⁴ found it present in 1 case; Thompson¹¹ observed it in 2 cases, and Rossi and Cova⁹ in 4 cases.

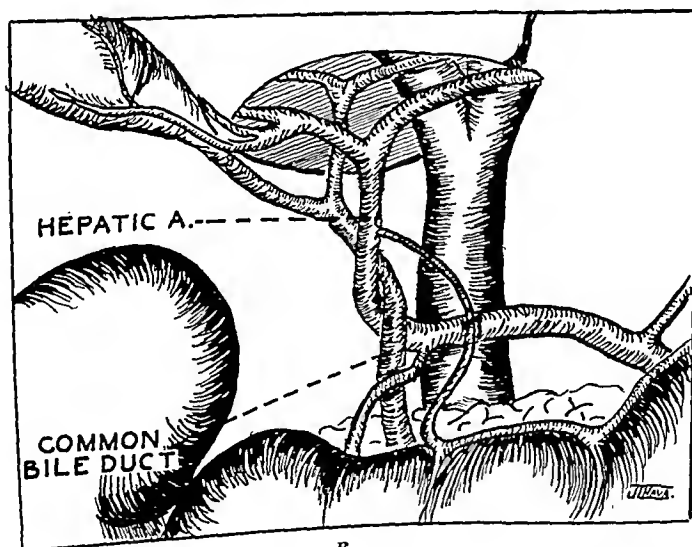
One passed behind the common bile duct (ductus choledochus) (Specimen 109, Fig. 1). A review of 1,700 cases collected from the literature reveals this case to be the only example in a common hepatic of celiac origin. Eight coursed in front of the common bile duct. Thompson¹¹ observed this in 1 case. The vessel coursed on the right side of the common duct in 1 case (Specimen 109, Fig. 1) and is apparently the only case of this type recorded in the literature. In five specimens the artery-

was found to pass ventral to the common hepatic duct (Specimen 270, Fig. 2). Thompson¹¹ found this in 2 of 50 cases.

The artery coursed in front of the cystic duct in Specimen 28. This is also the only case recorded of this relationship and is very important from a surgical viewpoint because of the liability of injury to the large vessel in securing this duct.



A.



B.

Fig. 1.—A, Specimen 88. Normal common hepatic artery passing posterior to the portal vein. The cystic artery courses in front of the common hepatic duct. B, Specimen 109. The artery passes behind the common bile duct, then on its right and ventral aspects.

B. *Absent*.—The common hepatic artery was absent in 14 specimens (5 per cent). In all of these the right and left lobes of the liver were supplied by a separate artery. Adachi,² Brewer,³ Kosinski,⁶ Lipshutz,⁸ and Thompson¹¹ found this present in 2 to 10 per cent of their cases.

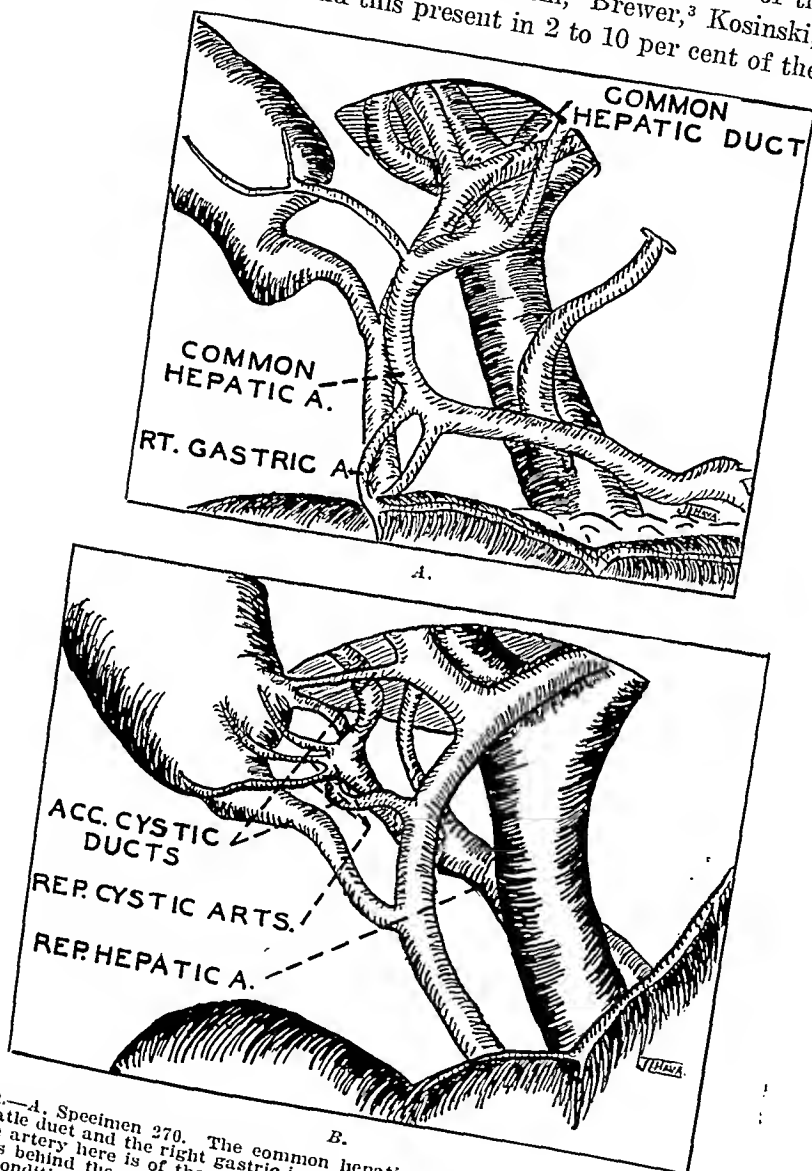


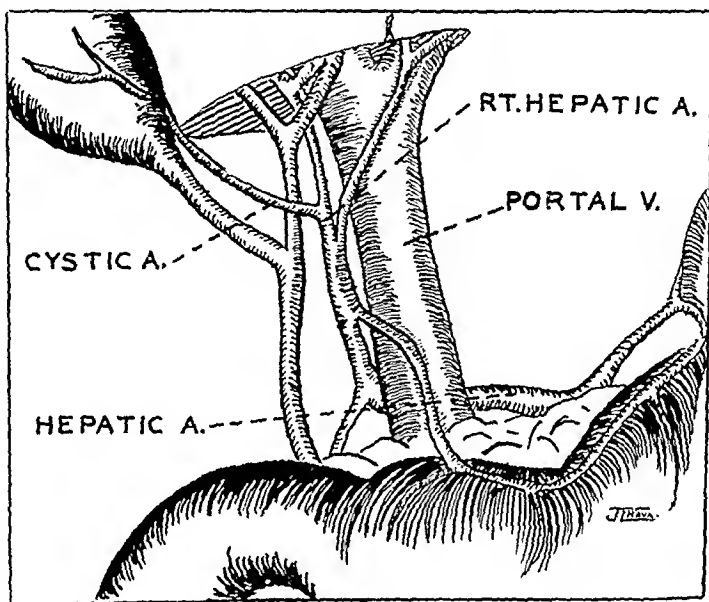
Fig. 2.—A, Specimen 270. The common hepatic artery courses ventral to the common hepatic duct and the right gastric in front of the ductus choledochus. B, Specimen 276. The artery here is of the replacing type, as it springs from the abdominal aorta. It courses behind the portal vein. Three replacing cystic arteries are shown (a very unusual condition).

B.

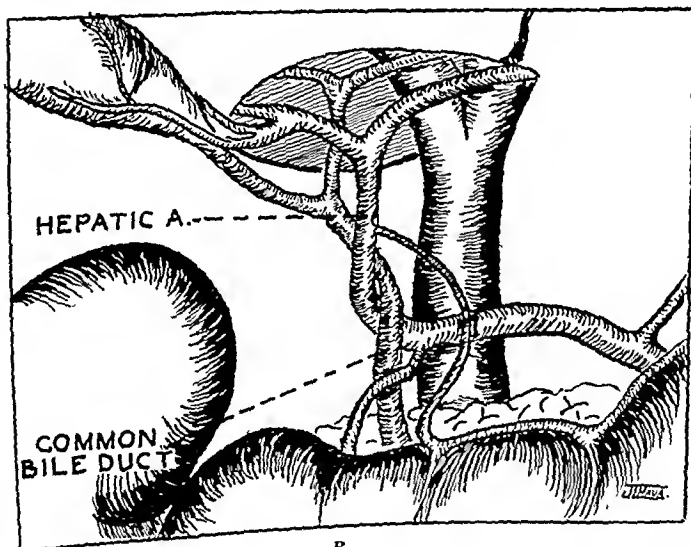
C. *One Replacing*.—This situation is present in 6 cases (2.2 per cent). Two of these arteries originated from the abdominal aorta and 4 from the superior mesenteric (Specimen 276, Fig. 2). Both of those originating from the abdominal aorta passed posterior to the portal vein. Three of the four from the superior mesenteric also passed posterior.

was found to pass ventral to the common hepatic duct (Specimen 270, Fig. 2). Thompson¹¹ found this in 2 of 50 cases.

The artery coursed in front of the cystic duct in Specimen 28. This is also the only case recorded of this relationship and is very important from a surgical viewpoint because of the liability of injury to the large vessel in securing this duct.



A.



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Fig. 1.—A, Specimen 88. Normal common hepatic artery passing posterior to the portal vein. The cystic artery courses in front of the common hepatic duct. B, Specimen 109. The artery passes behind the common bile duct, then on its right and ventral aspects.

E. *Two Accessory*.—This was not observed in my series of 280 specimens nor in those of other investigators. Some cases are mentioned in the literature of three hepatic arteries, but these cannot be classed as being definitely common hepatic vessels, so they are not considered under this heading. For instance, Segall¹² and Belou¹³ in their work with infusion methods show a few cases in which a moderate amount of fluid passes to the liver more or less indirectly from minute branches of the inferior phrenic and superior mesenteric.

GASTRODUODENAL ARTERY

From the studies of Vesale,¹⁴ a pioneer investigator, the conclusion was drawn that the gastroduodenal artery arose from the common hepatic artery in three separate stems. Winslow¹⁵ and Haller¹⁶ were the first to state that these three stems were branches of one gastroduodenal trunk which most often arose from the hepatic artery.

A. *Normal*.—In the present series of 280 cases the gastroduodenal artery arose normally in 220 (81.4 per cent) specimens. Fifty-eight (26.3 per cent) of these came off a short common hepatic trunk (*en bouquet* type) as one of the terminal branches, and 170 (77.2 per cent) came off a long trunk (classical type) as a first branch. These percentages of origin compare favorably with the findings of other investigators, which ranged between 80 and 96 per cent.

Sixty-two (27.6 per cent) of the vessels had an anterior relationship to the common bile duct in their entire course. This is an important relationship from the surgical point of view, especially during choledochotomy. Eisendrath¹⁷ found it present in 20 per cent of his cases and calls attention to its surgical importance. An exceptionally high incidence was reported by Thompson,¹¹ who found in the 40 cases of normally arising gastroduodenal vessels that 26 (65 per cent) coursed ventral to the common duct. His findings, however, emphasize the importance, already stated, of looking for this relationship in choledochotomy.

B. *One Replacing*.—This was present in 44 specimens and originated from the various vessels (Table II).

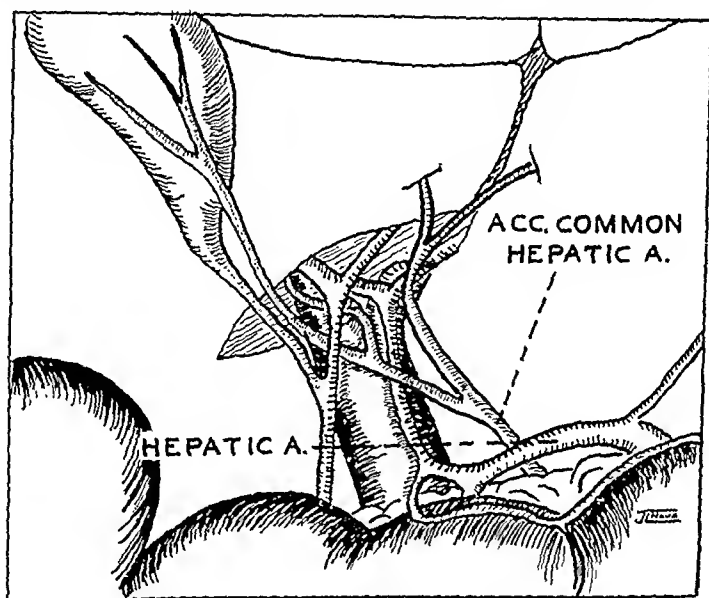
TABLE II

| SOURCE | FREQUENCY | PERCENTAGE OF REPLACINGS | PERCENTAGE OF WHOLE |
|--------------------------|-----------|-----------------------------|------------------------|
| Left hepatic | 2 | 4.54 | 0.7 |
| Right hepatic | 23 | 52.2 | 8.2 |
| Celiac (separately) | 1 | 2.2 | 0.35 |
| Replacing common hepatic | 4 | 9.1 | 1.4 |
| Replacing right hepatic | 2 | 4.54 | 0.7 |
| Replacing left hepatic | 12 | 27.3 | 4.2 |

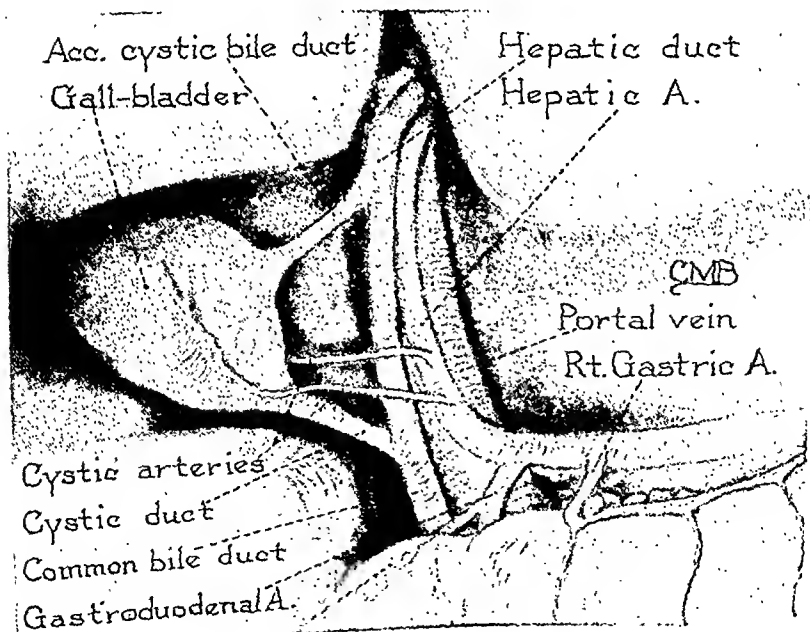
As compared with this, Adachi² found 32 cases in 252 specimens; Brewer,³ 7 cases in 50; and Thompson,¹¹ also 7 cases in 50.

In 44 of my cases, 32 coursed on the left side of the common bile duct and 12 coursed in front of this duct.

D. *One Accessory*.—This condition occurred in only 1 case (0.36 per cent) (Specimen 63, Fig. 3). From a perusal of the literature this condition also seems quite rare. Brewer's Specimen 6 should be included in this class, making 2 recorded specimens in 1,700 subjects.



A.



B.

Fig. 3.—A, Specimen 63. An accessory common hepatic artery from the superior mesenteric; a very rare condition. B, Specimen 187. Two replacing cystic arteries from the common hepatic; they course ventral to the common hepatic duct.

Branco,⁴ a contemporary of Wilkie,²¹ states: "There are two or three small branches which the gastroduodenal often supplies, quite near its origin. They go to the first portion of the duodenum on the superior border. They can originate from the proper hepatic (common) or from one of the terminal branches."

Flint²⁰ (1918) speaks interestingly of this vessel "which crosses the front of the supraduodenal portion of this duet (choledochus). Surgeons know it well and I was curious, therefore, to discover its source. I am unable to give the frequency of its existence, as I did not begin to look for it from the first, but I found it quite often." It was his surgical experience that it often caused annoying hemorrhage in opening the common duct.

Eisendrath¹⁷ (1918) is also evidently referring to this artery when he speaks of an "anomalous" branch of the gastroduodenal which he found in one of his specimens.

In my series of 280 specimens the artery was present in 56 (20 per cent) instances (Specimens 51 and 166, Figs. 5 and 6).

The source, frequency, and percentage of these vessels are shown in Table III.

TABLE III

| SOURCE | FREQUENCY | PERCENTAGE |
|------------------------------|-----------|------------|
| Gastroduodenal | 33 | 59.0 |
| Right gastric | 8 | 14.3 |
| Right hepatic | 5 | 9.0 |
| Common hepatic | 3 | 5.4 |
| Accessory right hepatic | 1 | 1.8 |
| Superior pancreaticoduodenal | 6 | 10.8 |

Twenty-five of the 56 vessels ran definitely anterior to the common bile duct, then entered the wall of the first portion of the duodenum and also supplied the lower extreme right end of the hepatoduodenal ligament. In the other cases (31 instances) the vessel began to terminate in the bowel wall before this anterior relationship was reached. In a few instances small branches were noted passing across the pyloric valve of the stomach. I agree with Thompson¹¹ that the artery has not received its due meed of esteem and feel that more mention of it should be made in textbooks of anatomy and surgery. It will be interesting to note what the future brings to light on this subject.

RIGHT GASTRIC ARTERY

This vessel was first described by Vesale¹⁴ and called by him the pyloric. It remained for Winslow¹⁵ and Haller¹⁶ to make a much more exact description, both as to origin and course. It was called by them "coronaria dextra minor." Later investigators began calling it by the name of right gastric and this is the name most used today.

A. *Normal*.—In the average textbook of anatomy this artery is described as branching from the common hepatic (after the latter vessel

C. *Two Replacing and One Accessory*.—None from these two categories was found present in my cases. It seems that so far no one has been able to find an example of multiplication of the trunk of this vessel.

D. *Absent*.—This occurred in 8 specimens (2.86 per cent). In each case the regions normally supplied were cared for by the left gastropiploic from the splenic, the inferior pancreaticoduodenal, from the superior mesenteric, and collaterals from the hepatic. This may have been the reason Vesale¹⁴ conceived his idea of the gastroduodenal as arising separately in three trunks.

SUPRADUODENAL ARTERY

During the beginning of this study, frequently there was observed a vessel supplying the first part of the duodenum, generally having its origin in the gastroduodenal artery and coursing anterior to the supraduodenal portion of the common bile duct. No mention of this vessel was made in any of the anatomy textbooks consulted, although some references to it were found in the works of Eisendrath¹⁷ and Flint,²⁰ and a more definite description of it is given in the works of Wilkie²¹ and Thompson.¹¹

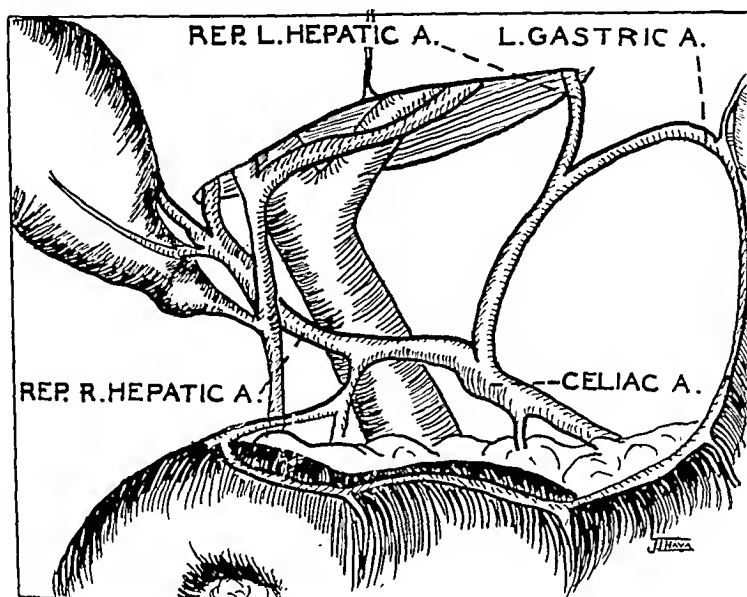
Wilkie²¹ speaks of this vessel as "a trunk which had its origin at a higher level than the midpoint of the gastroduodenal artery." He then states: "This vessel I ventured to call the supraduodenal artery." To ascertain its origin he injected various vessels of the upper abdomen in 40 fresh autopsy specimens with a mixture of starch and vermilion and, though he found the source of origin varied, most frequently it sprang from the gastroduodenal. But "whatever its origin, the artery soon divides into several branches. One of these (usually small) runs up into the gastrohepatic omentum; the larger branches descend to the anterior wall of the duodenum, one or more smaller branches going to the upper part of the posterior wall (of duodenum)."

Of especial interest to the surgeon is the observation Wilkie²¹ makes that damage to this vessel usually results in the development of duodenal ulcer in the area supplied by the artery.

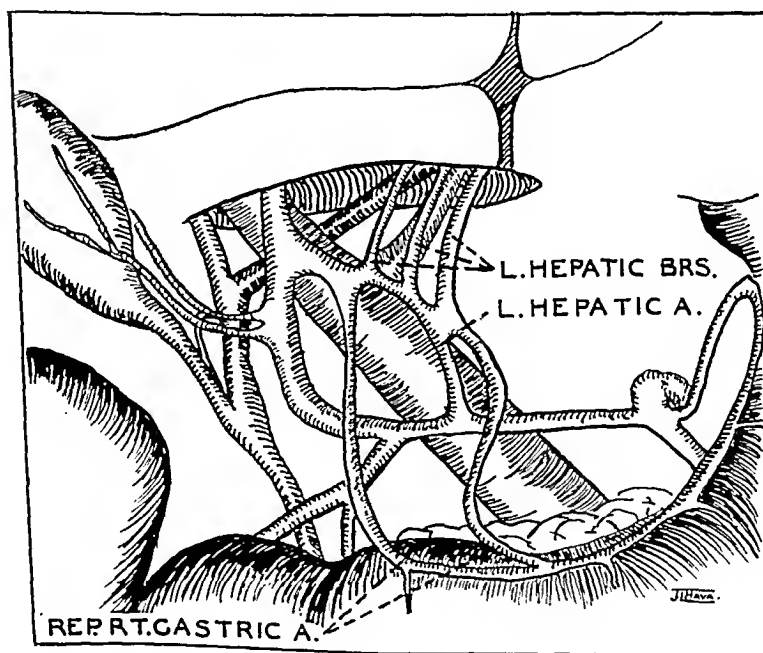
Thompson,¹¹ writing twenty-two years later than Wilkie,²¹ found the vessel in 14 per cent of his 50 specimens and used the term supraduodenal (as Wilkie suggested). He also drew attention to the surgical importance of its frequent anterior relationship to the supraduodenal portion of the common bile duct, as this relationship occurred in over 25 per cent of the vessels found.

Brewer,³ writing eleven years before Wilkie,²¹ evidently must have seen this artery, as he says: "Well-developed branches, capable of giving rise to annoying hemorrhage, were found arising from the gastroduodenalis and accompanying the common duct for a variable distance in eleven cases. Nine of these vessels were of considerable size and gave branches to the gall bladder, to the liver, or both." A fair description of the vessel is thus given, but he gave it no name.

ated left umbilical vein and was posterior to the left hepatic duct. In none of my specimens was the artery found dorsal to the portal vein. Thompson¹¹ is the only one reporting such a relationship.



A.



B.

Fig. 4.—A, Specimen 37. The left lobe of the liver is supplied by a replacing left hepatic artery from the left gastric. The replacing right hepatic is directly from the celiac. B, Specimen 133. Two replacing right gastric arteries, springing from the left

has entered the lower portion of the hepatoduodenal ligament) on the distal side of the origin of the gastroduodenal branch.

In the present series of 280 specimens the right gastric originated from the common hepatic artery in only 118 (42.2 per cent). Thus, the so-called "normal" origin is found to be erroneous.

Twenty-five of these normal vessels coursed ventral to the trunk of the gastroduodenal artery, and 22 had an anterior relationship to the common hepatic artery. Only 1 was ventral to the common bile duct (Specimen 270, Fig. 2).

B. One Replacing.—This was found to be more common than the so-called normal type; as it occurred in 126 (45 per cent) of 280. The most frequent source of origin of this vessel was the gastroduodenal and the next most frequent was the left hepatic artery, these two constituting over four-fifths of the total.

Five vessels coursed anterior to the common bile duct; 14 ran ventral to the gastroduodenal artery, and 26 pursued a course anterior to the common hepatic artery.

Adachi² found 69 cases of a one replacing right gastric artery in 191 specimens; Brewer,³ 11 in 50; Descomps,⁵ 54 in 124; Leriche and Villemain,⁷ 2 in 55; Rossi and Cova,⁹ 46 in 101; Yabuki,²² 12 in 32; Lipsechutz,⁸ 28 in 83; Thompson,¹¹ 12 cases in 50 subjects studied.

C. Two Replacings.—This condition was present in 4 cases (1.43 per cent). Fig. 4 (Specimen 133) shows both vessels coursing from the left hepatic artery. Branco⁴ is the only other investigator who found vessels of this type. In his 1 case, one vessel sprang from the left hepatic artery and the other from the right hepatic.

D. One Accessory.—Brewer³ and Lipsechutz⁸ report cases belonging to this category. This was present in 4 (1.43 per cent) of my series.

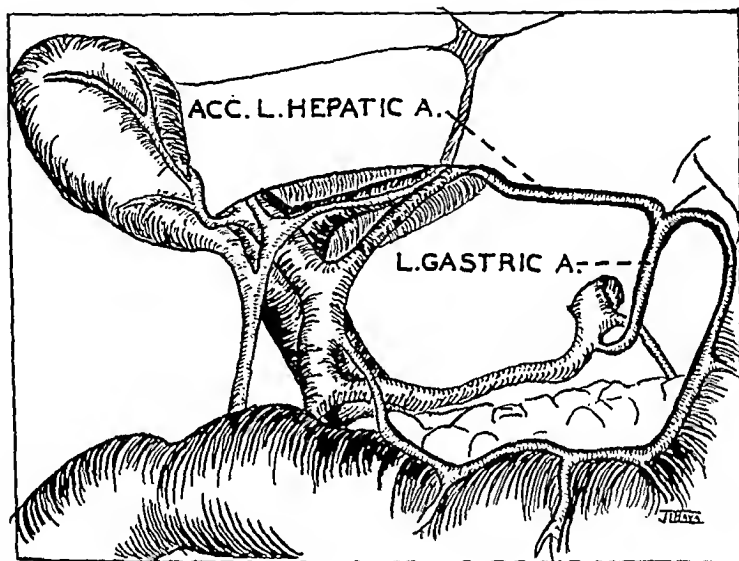
E. Absent.—This occurred in 28 (10 per cent) of 280 cases studied. It is possible that the vessel may have been present in some of these cases and overlooked. However, if it were, the artery was so small that it could be classed as negligible anyway. This condition was also found fairly frequently in the works of others. Thompson,¹¹ for instance, cites an incidence as high as 34 per cent and Brewer,³ one of 24 per cent. This information may be of value to those performing gastrectomies.

LEFT HEPATIC ARTERY

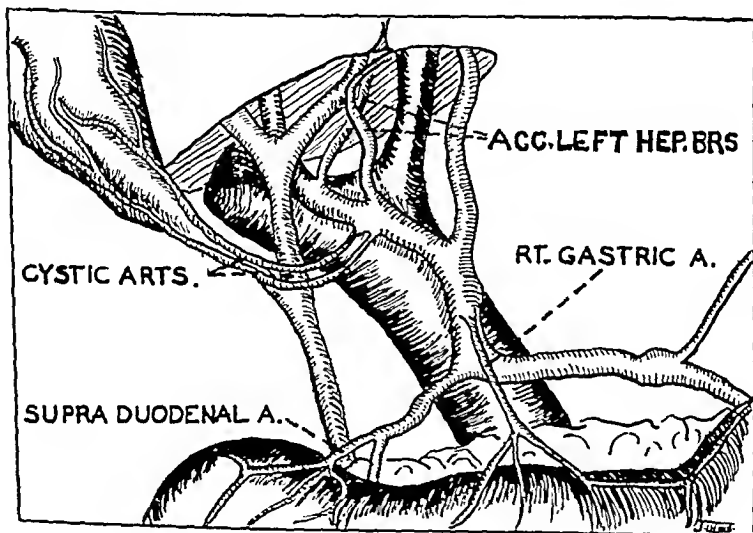
A. Normal.—In this series of 280 specimens, the left hepatic was found arising from the normal common hepatic only 188 times (66.7 per cent). Most of the other investigators in this field report figures well above 80 per cent; thus a considerable variation from the usual description was found, as far as the origin was concerned.

In 5 instances the vessel coursed anterior to the common hepatic duct, and in 1 instance it passed posterior to this duct. In 4 cases the vessel passed anterior to the right hepatic artery, due to the tortuous course of this latter vessel. Just before entering the liver it uniformly had an inferior relationship to the left branch of the portal vein and the obliterated

Numerous cases of abnormal course were found present in my series. Two passed behind the portal vein in a most unusual relationship (Specimen 266, Fig. 6). Six coursed anterior to the common bile duct (Specimen 166, Fig. 6), and 55 passed anterior to the common hepatic duct. In 4 cases the artery was found anterior to the cystic duct and in 15 it passed posteriorly. In 44 it closely paralleled this duct to the neck of the gall bladder, before turning upward or backward to the right lobe of the liver (Specimen 176, Fig. 7). This relationship is very important



A.



B.

Fig. 5.—A, Specimen 259. An accessory left hepatic artery from the left gastric. B, Specimen 51. Supraduodenal artery, arising from the gastroduodenal, courses in front of the common bile duct. An accessory cystic artery and two accessory left hepatics are also present.

B. One Replacing.—This occurred in 19 specimens (6.8 per cent). In 12 instances the anomalous vessel sprang from the celiac separately. In 1 case it came directly from the aorta; in 2 it originated from the aorta by means of a replacing common hepatic artery; in 3 it came from the superior mesenteric by means of a replacing common hepatic; and in 1 it originated from the left gastric artery (Specimen 37, Fig. 4).

One vessel coursed posterior to the bile ducts, and one passed in front of the common hepatic duct. Three coursed in the left portion of the lesser omentum, the portion known as the gastrohepatic ligament.

C. One Accessory.—Consistent with the method of classification used, 71 (25.3 per cent) accessory left hepatic arteries were found.

The source of origin of this accessory vessel was found to be considerably varied in my cases, as is shown in Table IV.

TABLE IV

| SOURCE | NO. OF CASES FOUND | PERCENTAGE |
|---|--------------------|------------|
| Right hepatic artery | 59 | 83.0 |
| Left gastric | 3 | 4.2 |
| Right gastric | 2 | 2.8 |
| Gastroduodenal | 1 | 1.4 |
| Celiac (separately) | 1 | 1.4 |
| Aorta (directly) | 1 | 1.4 |
| Superior mesenteric (accessory common hepatic branch) | 1 | 1.4 |
| Cystic | 2 | 2.8 |

Space will not permit the sketching of but one of these specimens (Specimen 259, Fig. 5).

In 1 case the accessory vessel passed posterior to the portal vein; one coursed in front of the common bile duct, and three in front of the common hepatic duct.

D. Two Accessory.—Only 1 case definitely showed this occurrence (Specimen 51, Fig. 5). A search of the literature shows this elsewhere only in 2 cases of Brewer³ and in 2 of Budde.²³

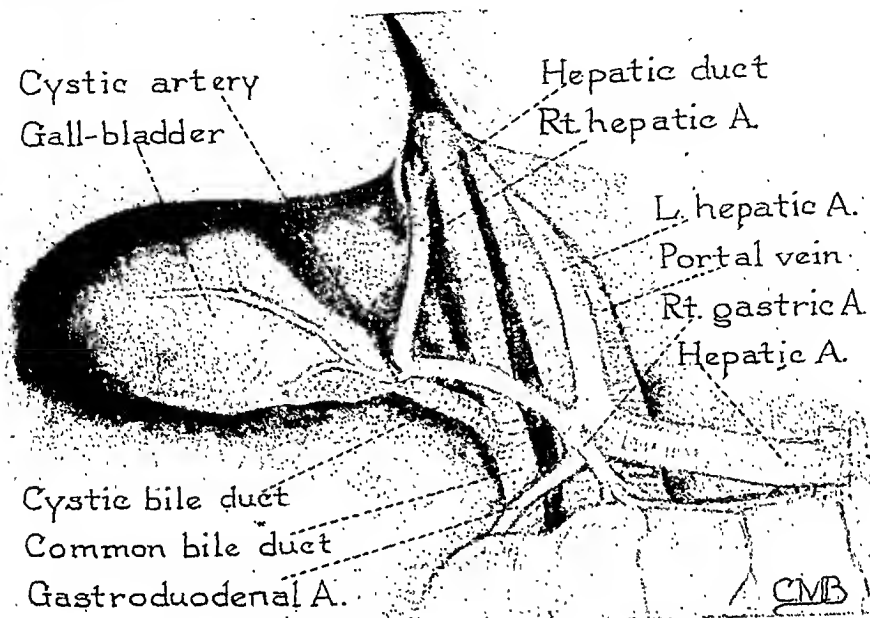
RIGHT HEPATIC ARTERY

A. Normal.—This occurred in 223 (79.7 per cent) of the 280 cases. This compares with other investigators as shown in Table V.

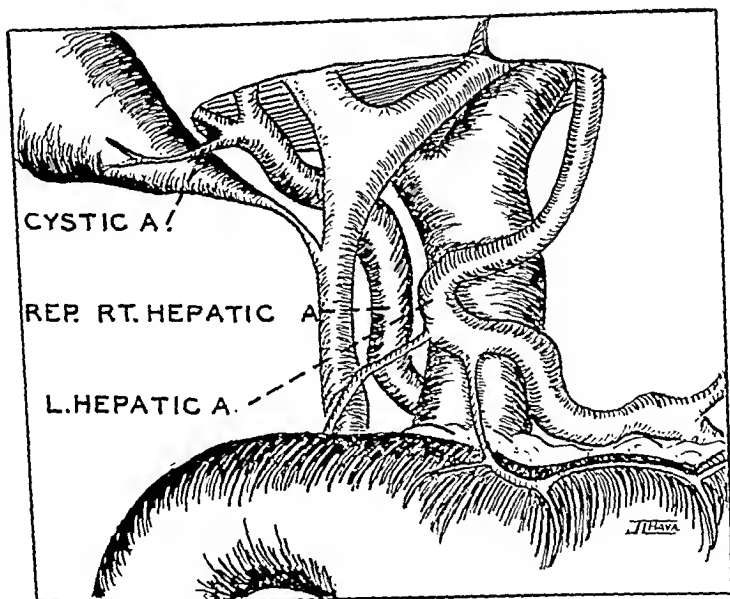
TABLE V

| AUTHOR | CASES EXAMINED | FREQUENCY | PERCENTAGE |
|-----------------------------|----------------|-----------|------------|
| Adachi ² | 252 | 221 | 87.7 |
| Branco ⁴ | 50 | 41 | 82.0 |
| Brewer ³ | 50 | 39 | 78.0 |
| Descomps ⁵ | 50 | 45 | 90.0 |
| Flint ²⁰ | 200 | 158 | 79.0 |
| Kosinski ⁶ | 55 | 51 | 93.0 |
| Lipschutz ⁸ | 83 | 64 | 77.1 |
| McWhorter ²⁴ | 37 | 32 | 86.5 |
| Rossi and Cova ⁹ | 102 | 92 | 85.5 |
| Susloff ¹⁰ | 131 | 112 | 85.5 |
| Thompson ¹¹ | 50 | 44 | 88.0 |
| Browne | 280 | 223 | 79.0 |

times in 50 cases and Thompson¹¹ found it 12 times in 50. Ritter,²⁵ by experimentation, found that necrosis occurs in practically every case where a terminal branch of the common hepatic was ligated and that this accident is fraught with more danger than the ligation of the main trunk



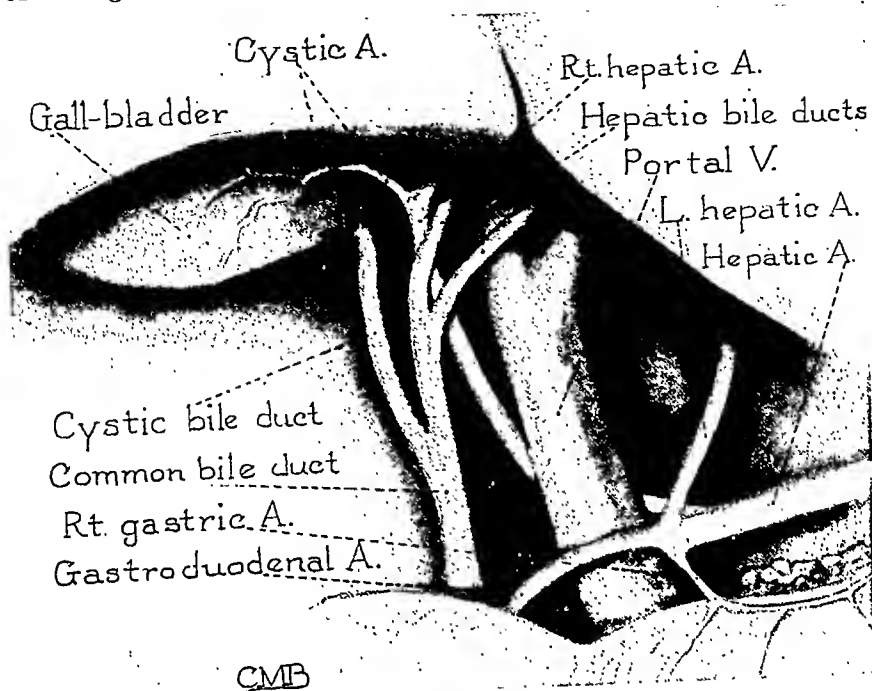
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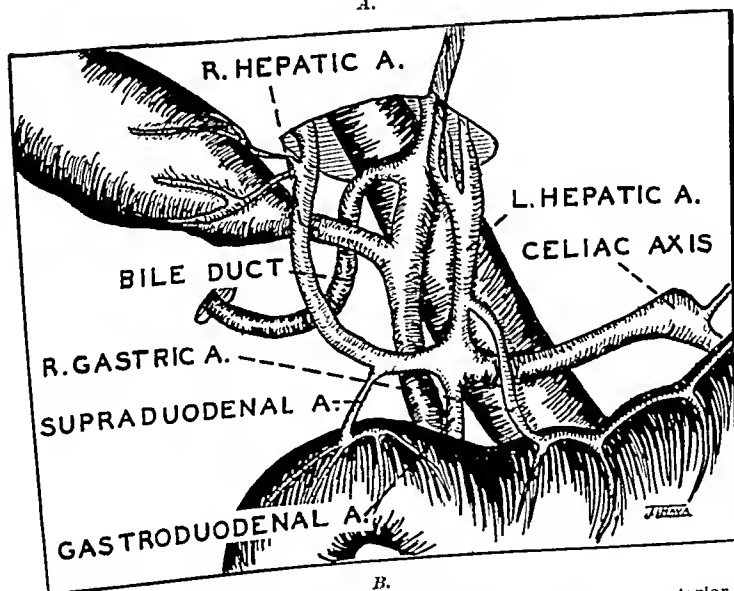
B.

Fig. 7.—A, Specimen 176. The right hepatic artery parallels the cystic duct to the neck of the gall bladder and gives off an extremely short cystic artery. B, Specimen 280. A replacing right hepatic artery from the abdominal aorta courses behind the portal vein and also parallels the cystic duct to gall bladder neck before giving off short cystic branch.

from the surgeon's viewpoint, as the vessel could be easily ligated while attempting ligation of the cystic artery, thus causing extensive necrosis of the right lobe of the liver. Brewer³ found this condition present 20



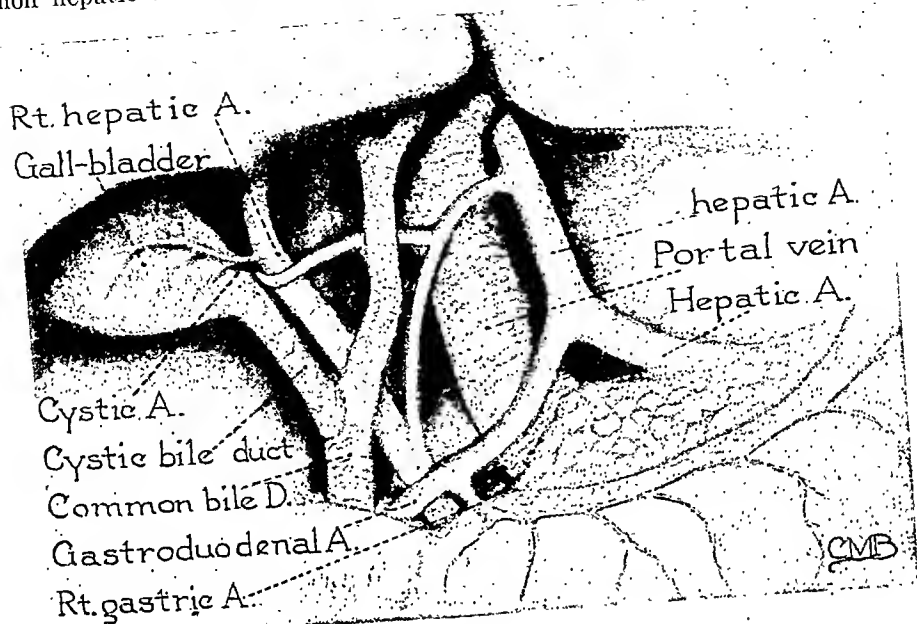
A.



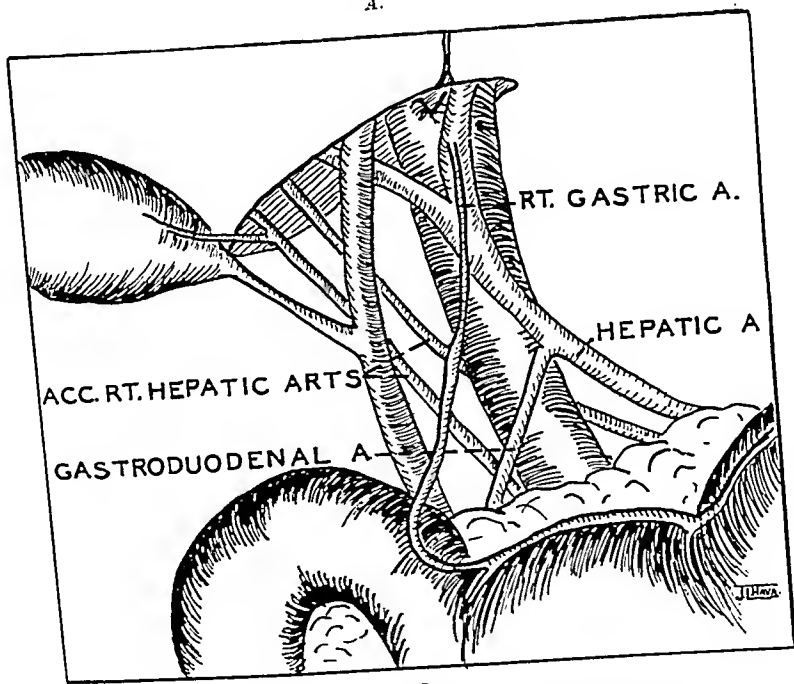
B.

Fig. 6.—A, Specimen 266. The normal right hepatic artery passes posterior to the portal vein. B, Specimen 166. The right hepatic courses in front of the ductus choledochus and the neck of the gall bladder. A very short cystic is to be noted, also a supraduodenal branch.

A. *Normal*.—The cystic artery is classified as normal in the usual text-book when it comes off the right hepatic in the angle between the common hepatic and cystic ducts, just as the right hepatic emerges from



A.



B.

Fig. 8.—A, Specimen 171. Accessory right hepatic artery from abdominal aorta parallels cystic duct and gives off short cystic branch. Note danger in surgery. B, Specimen 118. Two accessory right hepatic arteries from abdominal aorta; both course posterior to the portal vein.

of the artery. Mirizzi,²⁶ in his review of cases in the literature where this happened, also shows the unhappy results attendant in most of the incidents. Flint,²⁰ Eisendrath,¹⁷⁻¹⁹ and Friend,²⁷ as well, stress the frequency of this parallelism of the right hepatic artery to the cystic duct and consider the relationship most important from a surgical viewpoint.

In one case the right hepatic passed posterior to the common hepatic artery, which was due to the tortuosity of the latter vessel.

Compared with my 2 cases passing behind the portal vein, McWhorter²⁴ found 3 in 37 cases; Thompson,¹¹ 5 in 50; and Flint,²⁰ 4 in his 200. Compared with my 6 cases passing anterior to the common bile duct, Brewer³ found 1 in 5, which seems to be the only other case of this recorded. Thompson¹¹ found 5 cases passing anterior to the common hepatic duct, Brewer³ 7, Descomps⁵ 13, McWhorter²⁴ 5, and Flint²⁰ 25. Brewer³ and Thompson¹¹ each record 1 case of an anterior relationship to the cystic duct. The 1 case in my series of the artery passing posterior to the common hepatic artery seems to be unique.

B. One Replacing.—This was found present in 19 cases. Eight of these vessels originated from the abdominal aorta, 9 from the superior mesenteric, and 2 from the celiac directly (Specimen 37, Fig. 4). Thirteen of my 19 cases coursed posterior to the portal vein. This high percentage seems to be a fair index of the usual course of these replacing right hepatics. In 7 cases the vessel passed posterior to the common bile duct. Eight were posterior to the cystic duct; 1 was anterior, and 1 closely paralleled the cystic duct on its upper left aspect as far as the neck of the gall bladder (Specimen 280, Fig. 7). It is readily seen that about 50 per cent of these vessels would offer potential possibilities of damage during cholecystectomy.

C. Two Replacing.—No instance of this was found in my specimens and apparently not in the works of others.

D. One Accessory.—This occurred in 37 cases (13.2 per cent). The most common source of origin was the left hepatic (42 per cent). These accessory branches from the left hepatic were definite, large branches to the right lobe and could not be classed as a "ramus medius." Thirteen originated from the superior mesenteric and 9 from the abdominal aorta (Specimen 171, Fig. 8). Twenty-two coursed behind the portal vein and 3 coursed ventral to the common hepatic duct. As regards the cystic duct, 13 were in a dorsal relationship and 6 coursed parallel to the neck of gall bladder (Specimen 171, Fig. 8). This adds to the number which show this relationship so important surgically.

E. Two Accessory.—This was found present in 1 case (Specimen 118, Fig. 8). Brewer³ reports 1 case of this condition and there is also 1 case of Meckel's.^{28, 29}

CYSTIC ARTERY

Last, but not least, the cystic artery is a most important vessel from a surgical point of view and was found in my studies to show a large percentage of variations, only exceeded by the right gastric.

other references in the literature to this condition, but its full discussion here is inadvisable.

C. *One Replacing*.—This anomalous condition was present 46 times and the course of origin was extremely varied. Nine cases were from

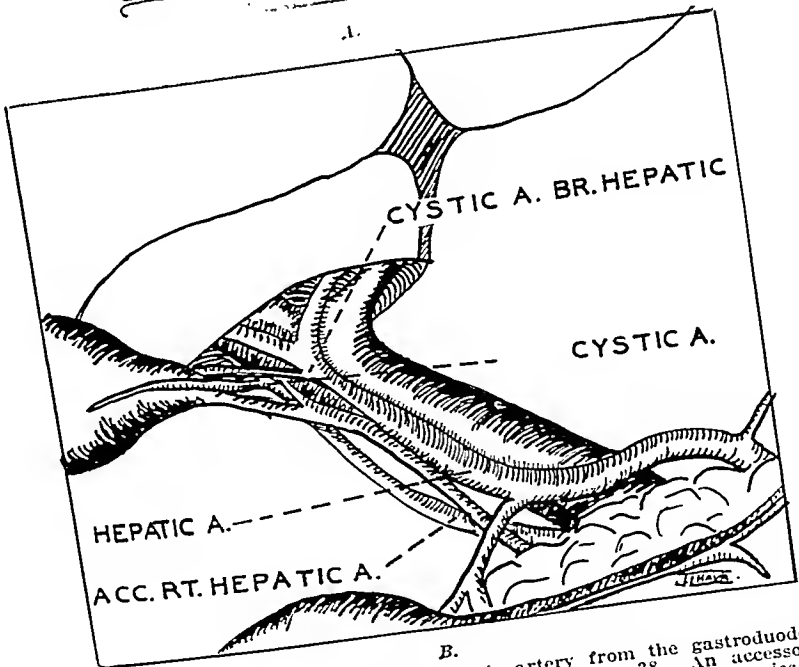
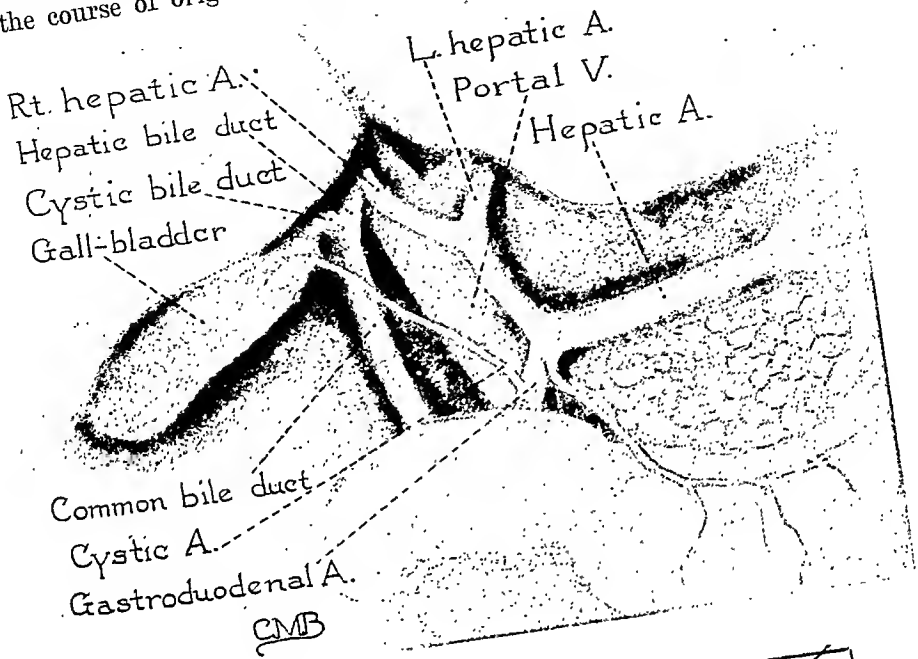


FIG. 2.—A, Specimen 265. Replacing cystic artery from the gastroduodenal. It courses ventral to the ductus choledochus. B, Specimen 38. An accessory right hepatic artery from the superior mesenteric and two replacing cystic arteries.

behind the common hepatic duct. In the present series this "normal" condition prevailed in only 153 cases (54.7 per cent).

The reports of other investigators may be compared with this low finding in Table VI.

TABLE VI

| AUTHOR | CASES EXAMINED | FREQUENCY | PERCENTAGE |
|-----------------------------|----------------|-----------|------------|
| Belou ¹³ | 150 | 104 | 70.0 |
| Branco ⁴ | 50 | 38 | 76.0 |
| Brewer ³ | 50 | 33 | 66.0 |
| Descomps ⁵ | 50 | 44 | 88.0 |
| Eisendrath ¹⁷⁻¹⁹ | ? | ? | 85.0 |
| Flint ²⁰ | 200 | 165 | 82.5 |
| Kosinski ⁶ | 55 | 51 | 93.0 |
| Lipschutz ⁸ | 83 | 54 | 65.0 |
| McWhorter ²⁴ | 37 | 34 | 92.0 |
| Rossi and Cova ⁹ | 96 | 79 | 82.3 |
| Susloff ¹⁰ | 118 | 96 | 81.3 |
| Thompson ¹¹ | 50 | 34 | 68.0 |
| Yabuki ²² | 29 | 26 | 89.6 |

The artery coursed ventral to the common hepatic duct in 37 cases (24 per cent) (Specimen 88, Fig. 1). Eisendrath¹⁷⁻¹⁹ stresses the surgical importance of this relationship and says it is present in 27 per cent of all cases. Flint²⁰ found it occurring 31 times out of 165; Branco,⁴ 12 times in 50; Susloff,¹⁰ 24 times in 118; Descomps,⁵ 20 times in 50; McWhorter,²⁴ 6 times in 37; Adachi,² 28 times in 65; Brewer,³ 2 times in 50; Yabuki,²² 3 times in 29; and Thompson,¹¹ 8 times in 50.

In my series it coursed posterior to the common hepatic duct in only 2 cases. Brewer³ found this present 3 times in 50 cases; Adachi,² 1 time in 65; McWhorter,²⁴ 6 in 37; and Thompson,¹¹ 1 time in 50.

Three cases coursed anterior to the right and left hepatic ducts and 7 coursed ventrally to the duodenum. Thompson's¹¹ Specimen 44 is the only other case that could be found showing this relationship.

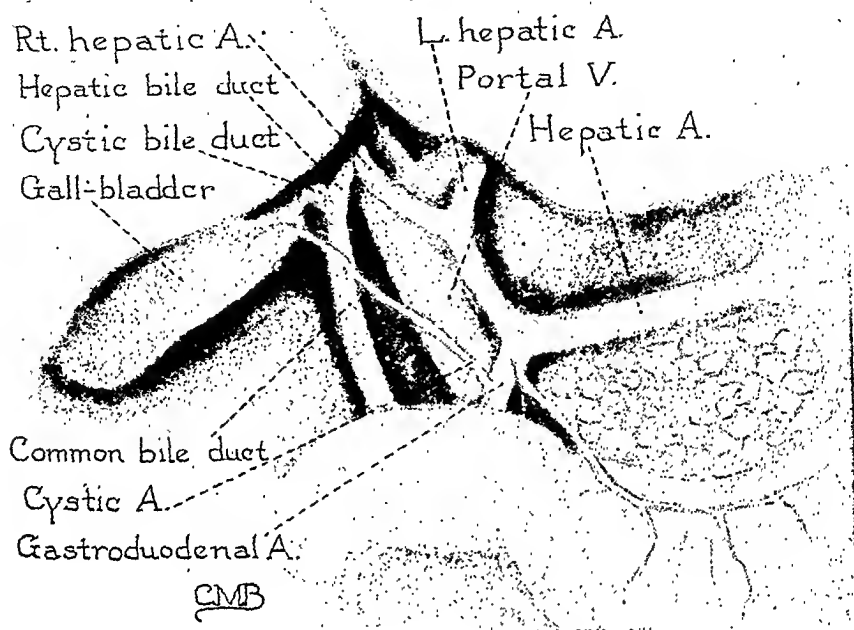
Thirty-seven (24 per cent) of these normal cystics had very short trunks, the vessel coming off the right hepatic practically on the neck or body of the gall bladder. This, as I have already stated, is very important from the viewpoint of the surgeon, as the right hepatic artery could be so easily ligated (or injured so severely as to require subsequent ligation), while attempting to ligate the cystic artery (Specimens 166 and 176, Figs. 6 and 7). Eisendrath,¹⁷⁻¹⁹ Friend,²⁷ and Flint²⁰ call especial attention to this fact in their articles.

No instance of a posterior relationship of the artery to the portal vein was found.

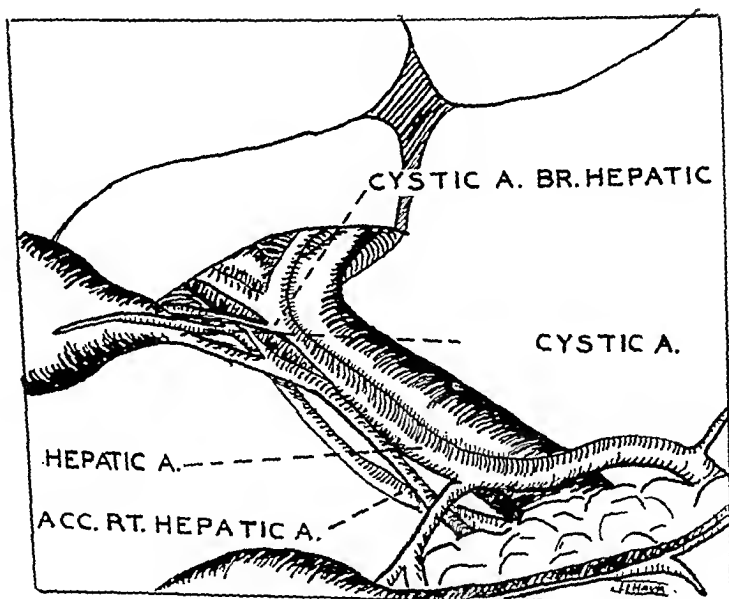
B. Absent.—This type is shown in 1 case (Specimen 60) and is a case of congenitally absent gall bladder. It is not a postsurgical condition, as no scar was present on the anterior body wall, the inferior surface of the liver, or the bile duct. The common duct was about three times the average size. The other vessels were found to be comparatively normal. Quenu³⁰ states: "The gall bladder is occasionally absent." Brewer³ states that Courvoisier has described a number of such cases. There are

other references in the literature to this condition, but its full discussion here is inadvisable.

C. *One Replacing*.—This anomalous condition was present 46 times and the course of origin was extremely varied. Nine cases were from



A.



B.

Fig. 9.—A, Specimen 265. Replacing cystic artery from the gastroduodenal. It courses ventral to the ductus choledochus. B Specimen 38. An accessory right hepatic artery from the superior mesenteric and two replacing cystic arteries.

the common hepatic artery; 5, from the left hepatic artery; 6, from the gastroduodenal; 11, from a replacing right hepatic artery; 9, from an accessory right hepatic; 3, from a replacing common hepatic; 2, from an accessory left hepatic; 1, from the superior pancreaticoduodenal artery; and 1, from the celiac directly.

Twelve of the vessels coursed anterior to the common hepatic duct and 8 passed anterior to the ductus choledochus (Specimen 265, Fig. 9). Nine of these vessels were also very short, coming off of their respective sources close to the body of the gall bladder (Specimen 280, Fig. 7). The surgical importance of this has already been stressed.

One of the vessels divided soon after its origin and coursed to the gall bladder as two separate stems. This, clinically at least, amounts to another case of an accessory cystic.

D. Two Replacing.—This was present in my series in 17 cases (6 per cent). Three cases show both anomalous vessels originating from the common hepatic trunk (Specimen 187, Fig. 3); 6 show both vessels originating from an accessory right hepatic; 6 show both springing from a replacing right hepatic; and 1 shows one of the vessels coming from the common hepatic and the other from an accessory right hepatic (Specimen 38, Fig. 9).

In 4 specimens both vessels coursed anterior to the common bile duct. In 5 instances one vessel was near the cystic duct (upper left aspect) and the other vessel was far removed from the duct. This would offer a potential source of trouble to the surgeon not suspecting the additional vessel.

E. Three Replacing.—This unusual condition was found in 1 specimen (Specimen 276, Fig. 2). The hepatic artery in this case was a branch of the superior mesenteric, so this placed the three cystics as replacing vessels. I was not able to find this condition reported in the work of any other investigator.

F. One Accessory.—This condition was present in 58 specimens (20.7 per cent). Forty-one of these accessory vessels originated from the right hepatic artery; 5 came from an accessory right hepatic; 2, from the left hepatic; 2, from an accessory left hepatic; 2, from the common hepatic; and 6, from the gastroduodenal (Specimens 51 and 77, Figs. 5 and 10).

In 5 cases the accessory vessel coursed anterior to the common bile duct (choledochus), and in 13 specimens it passed anterior to the common hepatic duct. These vessels are all important surgically, but those passing anterior to the bile ducts are especially so, the ducts so often being grasped with forceps in hurried efforts to control hemorrhage from the ent accessory vessel. Due to the fact that they are found in this position so often, all surgeons should look carefully for their presence during cholecystectomy.

G. Two Accessory.—In the present series Specimens 121, 138, and 144 show this most unusual condition very convincingly. The surgical importance of these cases is readily apparent (Specimen 121, Fig. 10).

Brewer³ also reported 1 case (Case 41). This makes 4 cases of this condition in approximately 1,700.

Before closing the consideration of the cystic artery, it may not be amiss to stress that double and multiple vessels were found in this series in practically one out of every three cases.

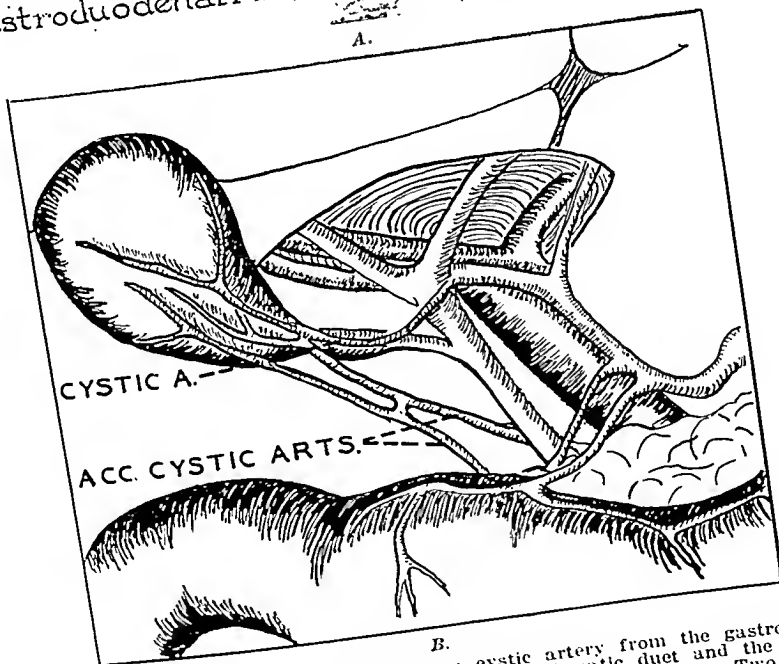
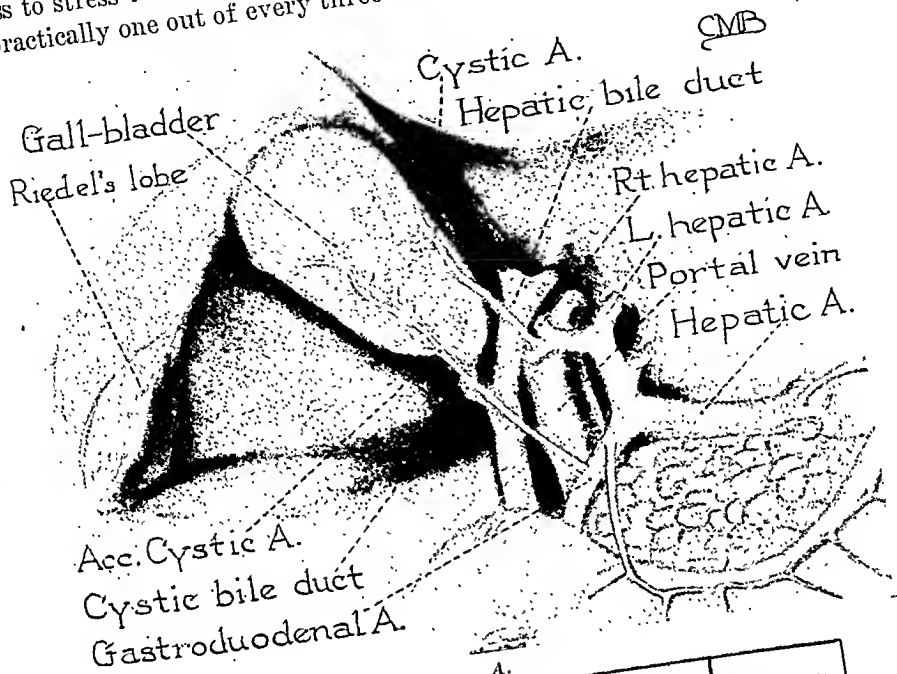


Fig. 10.—A, Specimen 77. An accessory cystic artery from the gastroduodenal. The normal cystic courses ventral to the common hepatic duct and the accessory cystic courses in front of the common bile duct. B, Specimen 121. Two accessory cystics, one from aorta and the other from the superior mesenteric. These are very unusual.

TABLE VII

| VESSEL | COMMON HEPATIC | | | | | |
|-----------------|----------------|-----------------|---------------|--------------|---------------|------------------------|
| | ARTERY | GASTRO-DUODENAL | RIGHT GASTRIC | LEFT HEPATIC | RIGHT HEPATIC | CYSTIC |
| Normal | 260—92.9% | 228—81.4% | 118—42.2% | 188—66.7% | 233—79.7% | 153—54.7% |
| Absent | 14—5% | 8—2.86% | 28—10% | 19—6.8% | 19—6.8% | 1—35% |
| One replacing | 5—1.3% | 44—15.7% | 126—45% | None | None | 46—16.5% |
| Two replacing | None | None | 4—1.43% | None | None | 17—6% |
| Three replacing | None | None | 4—1.43% | None | None | 1—0.35% |
| One necessary | 1—0.35% | None | None | 71—25.3% | 37—13.2% | 58—20.8% |
| Two necessary | None | None | None | 1—0.35% | 1—0.35% | 3—1.08% |
| | | | | | | Present 56 times (20%) |

In conclusion, I trust that this work will not be looked upon as simply another article on the hepatic artery. The field is big and it is hoped that this study will be an incentive for other investigators along this line.

My sincere thanks are extended to Dr. Wilbur C. Smith, professor of anatomy in Tulane Medical School; Dr. A. F. Reed, assistant professor of anatomy; Mr. Leo Faust and Mr. William M. Sherrill, student assistants in the department of anatomy, for their valuable help and sympathetic interest. Thanks are also extended to Miss Harryette Sprole, Mr. A. Greutert, and Mr. A. Vogt for assistance in translations.

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SUBCAPSULAR RUPTURE OF THE LIVER IN A CHILD

THOMAS F. CORRIDEN, M.D., NORTHAMPTON, MASS.

RUPTURE of the liver may be traumatic or spontaneous. Traumatic rupture may be due to direct or indirect violence. Accidents of direct violence are readily understood. According to Allesandri,¹ "indirect contusions may follow a fall upon the feet, the knees, or the buttocks, more rarely the head. Very exceptionally lesions of the liver are observed as the result of violent muscular exertion, as in the course of parturition or in epileptic seizures. In such cases it is usually necessary to assume a diminished resistance of the organ as a necessary condition."

The mortality in cases of ruptured liver has been variously given as 45 to 78 per cent. The most serious immediate feature is hemorrhage with sepsis as a complicating factor.

The literature on rupture of the liver following known severe injury is fairly extensive, and the mode of production of the rupture requires no explanation. Cases of spontaneous rupture or of rupture following indefinite or insignificant injury are less frequent. However, spontaneous rupture has been reported in a variety of pathologic conditions, such as carcinoma, syphilis, hemangioma, malaria, biliary tract disease, and toxic infections (Mast and Streamer,² Devie and Bériel,³ Marchstadt,⁴ McEwan and McEwan,⁵ Nauwerck,⁶ Sciacca,⁷ and others).

The explanation of the probable sequence of events that takes place in such cases, first advanced by Devie and Bériel,³ was later reaffirmed by Mazel:⁸ "In traumatic rupture, the rupture is the cause of the hemorrhage. In spontaneous rupture, the hemorrhage is the cause of the rupture. The chain of events leading to rupture are infarct, hypervascularization at the periphery, rupture of a vessel, intrahepatic hemorrhage with resulting rupture of the tissue and production of a subcapsular hematoma; when the pressure is great enough, rupture of the capsule permits escape of blood into the peritoneum leading to peritonitis and death."

Rupture of the liver in the newborn presents a somewhat different problem. The literature with discussion of etiology and relation to trauma has been reviewed by Hédren⁹ in 1917, Genell¹⁰ in 1930, and Silver¹¹ in 1938.

Instances of liver rupture occurring spontaneously in supposedly healthy liver tissue or after only trivial violence are perhaps of especial interest because the etiologic factors seem less apparent.

The large size of the liver and the fact that it contains little elastic tissue favor rupture of this organ as compared with that of the lungs, spleen, or kidneys. The relatively greater size in youth than in old age

may account for a greater incidence in younger individuals. Lamb²³ has analyzed sixty cases of rupture of the liver seen at the Boston City Hospital. Of this number, fifteen, or 25 per cent, were 10 years of age or younger. Springer¹² comments that in children even slight trauma may lead to a tear of a parenchymatous organ, due perhaps to relative weakness of the framework of connective tissue and to elasticity of the lower ribs.

Heinzellmann,¹³ in 1886, reported an instance in which a sudden acute anemia with death in a few minutes occurred in an 18-year-old boy convalescing from pneumonia. During the night of the fourteenth hospital day, another patient by accident lay down in the boy's bed. The boy either made a sudden movement in fright or the other patient may have rolled on him. Autopsy revealed a large hole, $1\frac{3}{4}$ inches in diameter in the liver. The hepatic tissue was described as "succulent."

In 1899, Carnabel¹⁴ described a case in a young man 26 years of age, admitted to the hospital for osteoperiostitis of the inferior maxilla. Two incisions were made. Six days after admission, the patient suddenly complained in the night of abdominal pain and epigastric cramps. A diagnosis of appendicitis was made the following day, but operation was postponed. During the second night the patient cried out suddenly and died. A posterior rupture 4 cm. deep was found in the liver.

The case of Bernard¹⁵ is often cited as one of spontaneous rupture of the liver, without even remote possibility of effort. A woman of 62 years was recovering from hemiplegia. Suddenly, in the midst of a conversation, she lost consciousness and died an hour and a half later from abdominal hemorrhage. At autopsy the liver capsule was found to be broken posteriorly with a cavity in the parenchyma as large as a small orange.

Devic and Bériel³ collected eleven cases of rupture of the liver from the literature. While some were definitely due to syphilis or cancer, in four there was no history of injury and no pathologic condition present as far as known.

Pichon and Cachin¹⁶ has occasion to operate upon a patient with rupture of the liver following a seemingly insignificant trauma. The patient was a man 34 years of age with no previous hepatic illness. The Bordet-Wassermann test was negative. He had a violent fit of coughing followed by a severe pain in the right hypochondrium and vomiting. The evening before he had performed some gymnastic exercises and had expended considerable effort in extension of the arms. At operation a rupture with a grayish border was found on the inferior surface of the quadrate lobe; the rest of the hepatic tissue appeared normal. The patient recovered.

Seiacea⁷ reported a case in which the liver apparently ruptured spontaneously during a normal bodily movement. The patient, a young priest, had been ill for about four weeks with an oral septic process. This was followed by a recurrence of fever and abdominal pain thought

to be due to a metastatic localization in an abdominal organ. After a period of convalescence, as he bent over in the lavatory, he was seized with a violent pain in the right upper quadrant. Death occurred in less than two hours. At autopsy a linear laceration 8 by 5 cm. was found in the right lobe of the liver. The liver was large, very soft, with a diffuse yellow coloring. No microscopic examination was made. Sciaeca reviewed the literature, including the reports of Heinzellmann, Bernard, Devic and Bériol, Pichon and Cahin described above. From a study of these cases, Sciaeca questioned whether sound hepatic tissue can rupture spontaneously. He concluded that, when rupture occurs with minimal cause, the parenchyma is probably not normal.

Another case of liver rupture following injury considered minor in character was reported by Robin.¹⁷ A man, 28 years of age, with a negative history of syphilis or any disease of importance, fell forward on his abdomen when the edge of the ditch on which he was standing gave way and struck the other side of the ditch. Operation about ten hours later revealed a laceration of the right lobe of the liver which penetrated deeply into the liver substance. Bleeding was profuse. The postoperative course was stormy, but the patient recovered.

Relatively few cases of the type under discussion have been reported in children. Bradley and Garrett¹⁸ describe an instance of spontaneous rupture of the liver in a child with complete recovery and believe it to be the only case of spontaneous rupture followed by recovery reported. A child, 3 years of age, became suddenly ill while eating breakfast, vomited, and grew feverish. X-ray, seven days later, showed an enlarged liver shadow. Laparotomy was performed sixteen days after onset of the illness. On opening the abdomen, an enlarged liver presented, with a bluish mass beneath a thin capsule; the capsule was ruptured; the liver had apparently ruptured previously and now enclosed a clotted mass. Most of this mass was removed, leaving a transverse irregular crater in the right lobe. This was packed with gauze. Convalescence was uneventful.

Springer¹² describes four cases of rupture of the liver. Two of these occurred in children, one 13 and one 8 years of age. The trauma in each instance was felt to be relatively slight: in the one case, a fall of three feet striking a diagonally placed stick with the right flank; in the other, the child slipped on some steps and struck the right flank on the corner of one step. A similar accident was mentioned by Lamb.²³ In Springer's cases, as in the one reported by Robin,¹⁷ the hemorrhaged blood suctioned from the abdomen, was used for autotransfusion according to the method advocated, so Robin states, by Theis in Germany in 1911.

It may be well to emphasize at this point that reinfusion of hemorrhaged blood is not without danger. Experimentally, Filatov¹² found that blood introduced into the pleural or peritoneal cavity of dogs underwent a progressive change. Evidence of hemolysis was apparent after

sixteen hours and quite marked at the end of twenty-four hours. Small amounts of this hemolyzed blood, when introduced intravenously, had no ill effects on the animals; but intravenous injections of quantities greater than 1.5 to 2 c.c. per kilogram of body weight resulted in a fall of blood pressure, albuminuria, hemoglobinuria, and oliguria.

Allen²⁰ reported a case of traumatic rupture of the liver. At operation three hours after the accident, 800 c.c. of blood was suctioned from the abdomen and injected intravenously. The patient died fifty-six hours later of complete anuria. Allen attributed the fatal outcome to the effect of the autotransfusion. In a discussion of subcutaneous abdominal injuries, Lewis and Trimble²¹ refer to this accident and suggest that the damage in such instances may be caused by the toxins elaborated by a ruptured liver in which autolysis takes place rapidly.

Watson and Watson²² have reviewed the American literature on autotransfusion. They collected 272 cases in which reinfusion of hemorrhaged blood was employed and reported two additional cases of their own. In many of the cases the procedure had been believed to be of marked value. Nonfatal reactions occurred in nine instances. Four cases were fatal; in three of these (cases of ectopic pregnancy) death was attributed directly to the autotransfusion. Of the total number of cases, six were instances of liver injury; no transfusion reaction was reported among these. Watson and Watson believed that untoward autotransfusion reactions are probably due to a toxin, perhaps free hemoglobin, which appears in the extravasated blood subsequent to the hemorrhage. These authors believed that the use of such hemorrhaged blood should be limited to cases where the demand is urgent and where there is no contraindication due to the age or source of the blood.

From a survey of the literature it is seen that cases of spontaneous rupture of the liver or of rupture following slight trauma are comparatively rare and those with recovery are even less frequent. In instances of apparently spontaneous rupture it would seem that the possibility of trauma antedating by some interval the appearance of acute symptoms and perhaps ignored at the moment should be borne in mind. During a period of intrahepatic hemorrhage and formation of a subcapsular hematoma, symptoms may be insignificant; but, when the capsule has ruptured, thus relieving the pressure that has partially controlled the hemorrhage, and free blood escapes into the abdomen, symptoms may become acute. This has been noted, according to Silver,¹¹ in the newborn; the child may be born apparently normal and may appear to be well until the third or fourth day, when there is sudden collapse and death.

It has seemed desirable, therefore, to present a case of subcapsular hemorrhage of the liver with recovery in a 9-year-old boy with an indefinite history of trauma of only moderate severity. The mother and father and two siblings younger than the patient were all living and well. There was no known history of syphilis.

CASE REPORT

E. J. P., aged 9 years, was admitted to the Cooley Dickinson Hospital, Sept. 23, 1939, complaining of pain in the right shoulder, arm and entire right side of two days' duration.

Except for scarlet fever, measles, and whooping cough, the boy had always been healthy.

On Sept. 21, the child came in from riding about 7 P.M. He felt well, undressed for bed, and went to the bathroom as usual when he complained of pain in the right side. He got into bed and then suddenly complained of pain in the right shoulder and entire right side and seemed in agony. He vomited a few minutes later. He was seen by the family physician and treated for an upset stomach. He was in severe pain throughout the night but was more comfortable in the morning and when examined again by the doctor presented no positive findings. The patient slept most of that day, but at 9 P.M. he had another acute attack of pain which lasted for three hours. He complained of pain at intervals during the night. On the morning of Sept. 23, the child was very pale and the pain was so severe that he wouldn't permit his parents to touch the right side of the abdomen. The boy was then taken to the hospital.



Fig. 1.—Appearance of the abdomen with incision.

No history of injury could be obtained at this time. Later, after diligent inquiry, several conflicting stories were obtained to the effect that the child fell from a tree, fell off a hay mow, was pushed off a swing in motion. None of these statements could be confirmed. The only story the mother believed might be true was that, on Sept. 18, two boys at school, younger than the patient, lifted the child up and threw him to the ground.

Examination at the hospital revealed a well-developed and well-nourished 9-year-old boy, who appeared seriously ill. The lips were pale. He was unable to take a deep breath because of pain in the right upper quadrant. There was no jaundice nor marks or bruises on the body. The rest of the physical examination was negative except for the abdomen. On inspection there was a large, round,

dome-shaped mass which extended from the right costal margin to the midline and resembled a small melon (Fig. 1). This mass was extremely tender. The lower abdomen was essentially negative except for marked tenderness. There was no definite spasm or rigidity. Impression: (1) cyst or abscess of the liver; (2) ruptured diverticulum of the small bowel or ruptured stomach; (3) hemorrhage of the liver.

Cyst was ruled out because of the rapidity of development; no mass had been present when the patient was examined by his physician two days previously. Against an abscess was the fact that there was no elevation of temperature. X-ray showed a dense shadow over the upper right abdomen but no air under the diaphragm, thus excluding rupture of a hollow viscus. The third diagnosis was made by elimination.

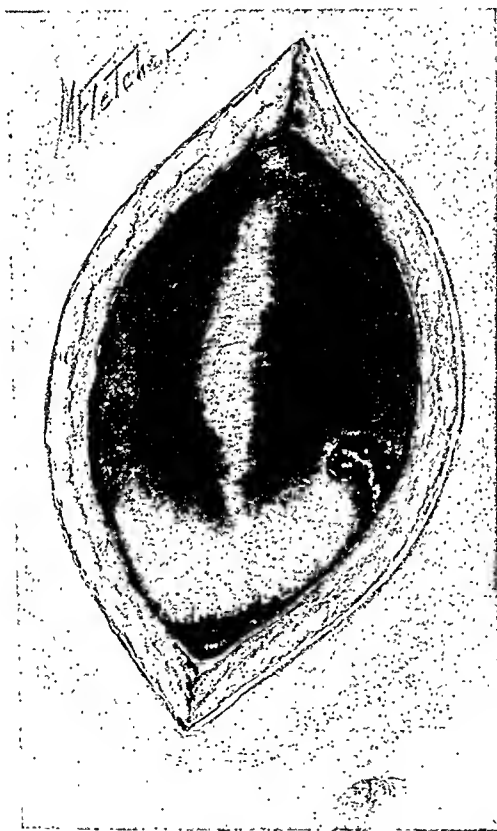


Fig. 2.—Hemorrhage from the ruptured capsule.

Laboratory Findings.—R.B.C., 3,490,000; hemoglobin (Sahli), 65 per cent; W.B.C., 19,900; neutrophils, 86; eosinophiles, 1; lymphocytes, 13; blood, Type A; Hinton test negative.

Operation was performed Sept. 23 shortly after admission. Under gas and ether, an incision which started well over the mass and extended down the right side almost to the level of the umbilicus was made and the abdomen opened without difficulty. The first impression was of a large domelike cyst (Fig. 2). A tremendous amount of dark red blood began to flow from the lower abdomen. Using suction, the blood was removed. The incision was extended upward and the liver carefully examined. At the junction of the anterior liver edge, to the right of the ligament and near its attachment, the tension had become so great that the

capsule had lifted up and through this opening had occurred the hemorrhage into the abdominal cavity. The diagnosis of a subcapsular hemorrhage of the liver was now established. Undoubtedly the pressure of the blood within the cavity in the liver parenchyma had acted as a tampon as long as the liver capsule was intact or nearly so. Otherwise death would have occurred within a short interval from massive hemorrhage into the abdomen.

A 3-yard wick was now placed above the liver, between the diaphragm and the liver, bringing the liver well down into view. Another wick was placed at the lower portion of the liver. During the manipulation the capsule ruptured with a large tear extending over the entire hemorrhagic portion of the liver; with the pressure thus released, marked hemorrhage ensued. Another 3-yard wick wet with

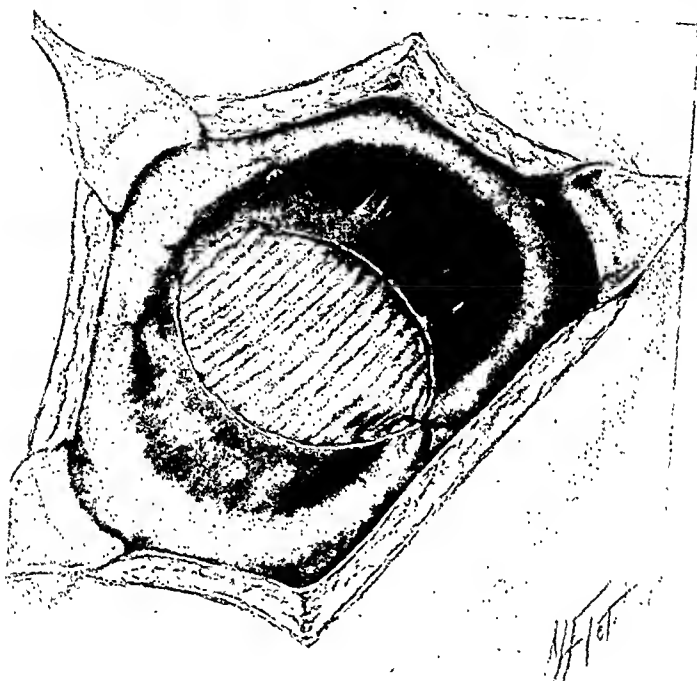


Fig. 3.—Muscle inserted into the liver cavity.

saline solution was hastily placed in this cavity which could now be seen to be 4 inches in length and about 3 inches in width, extending well down into the parenchyma of the liver. Pressure from the wick stopped the hemorrhage temporarily. With removal of the wick, the hemorrhage continued. It was then decided to excise the rectus muscle. About 5 inches of muscle were cut away and inserted into the liver cavity. Three sutures of plain catgut were loosely placed and the muscle was packed into the liver cavity as securely as possible. The omentum was then brought up and packed in over the muscle. The torn edges of the capsule were sutured with plain catgut. By this time the hemorrhage seemed to be fairly well under control. With the suturing of the capsule, a large 3-yard wick was placed between the capsule and the abdominal wall. All bleeding was controlled, the wick left in the abdomen, and the incision sewn with layer sutures using plain, chromic, and dermal. The boy's condition was poor; the pulse was barely perceptible. He was given an immediate transfusion of 500 c.c.

of citrated blood on the operating table. In about one-half hour his condition showed improvement. He was taken back to bed and put up on shock blocks. In the evening the temperature was 102° F.; pulse, 140; respirations, 20.

Following operation, the temperature showed a daily rise, spiking to elevations ranging from 102 to 105.2° F. Drainage, apparently of old blood, practically ceased on Sept. 24 but began again on Sept. 27. Transfusions were repeated on Sept. 24 and 27. Snake venom, 0.5 c.c., was administered on Sept. 27 and medication of klotogen instituted. The patient's condition was poor and he was placed in an oxygen tent.

By Sept. 30 the boy had definitely improved. The next day the 3-yard wick was removed; withdrawal was followed by drainage of a small amount of dark-colored blood.

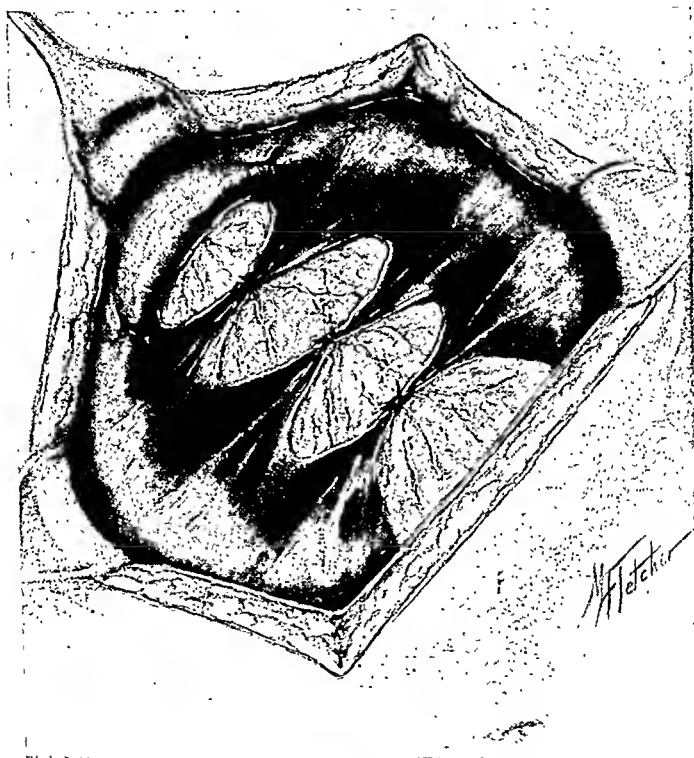


Fig. 4.—Omentum of muscle and suturing of the capsule.

From Oct. 2 to 5, the temperature continued to spike and the patient complained at intervals of pain in the right shoulder. Examination revealed signs of fluid in the right pleural cavity, confirmed by x-ray. A small trocar was inserted and 3.5 ounces of foul-smelling burgundy-colored fluid were obtained. A catheter was inserted and sutured to the chest wall. Culture of the pleural fluid showed hemolytic streptococcus as the predominating organism. Administration of neoprontosil was begun.

The patient's condition again improved; the temperature fell to a lower level. By Oct. 10 x-ray showed that the right lung had expanded and that very little fluid remained in the pleural cavity. The next day, however, the temperature again began to spike up to 104° F. and there was evidence of abdominal distress. On Oct. 12 a Kelly clamp was inserted into the old drainage area in the abdomen. A considerable amount of foul-smelling pus was discharged. On culture, hemolytic

streptococcus was found to be the predominating organism. On Oct. 13 the clamp was reinserted into the abdominal incision and two large catheters were placed in the wound between the liver and abdominal wall. During this procedure there was a discharge of 8 to 10 ounces of foul-smelling dark fluid. This relieved the abdominal discomfort. Neoprontosil had been discontinued on Oct. 10 but was resumed because of the secondary infection.

The boy then began to improve steadily. By Oct. 20 the temperature was normal; there was almost no discharge from the abdominal wound; there was no cough; and the patient was on a regular diet. He was discharged from the hospital on Nov. 8, having apparently made a complete recovery.

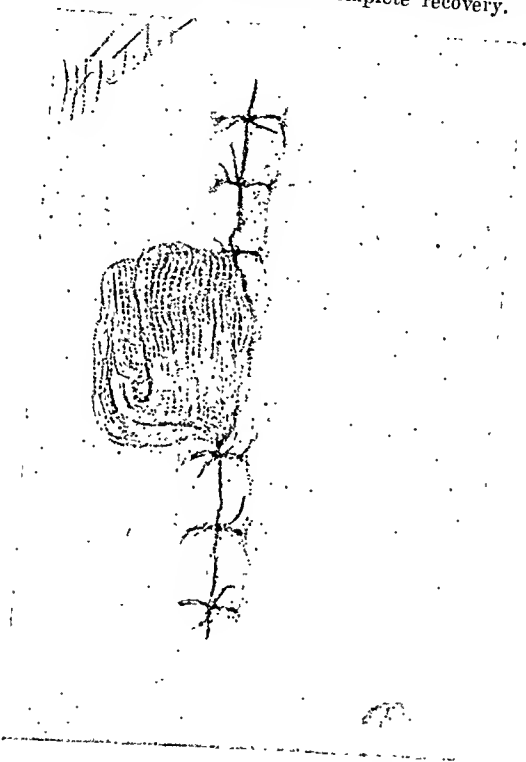


Fig. 5.—Closure of the wound with drain.

Repeated blood counts were made during the illness. The lowest red count was 3,130,000 on Sept. 25, with a hemoglobin (Sahli) of 60 per cent; the red cells showed marked polychromatophilia. At the height of the infection the white count was 25,500, with 96 per cent neutrophils. The coagulation time (capillary tube) on several examinations was 4 minutes. On Oct. 16 the red count had risen to 4,080,000; the hemoglobin (Sahli) was 83 per cent, white cells 11,900 with 59 neutrophils, 2 basophils and 39 lymphocytes.

SUMMARY

1. The literature on rupture of the liver, both spontaneous and following only trivial violence, has been reviewed.

2. A case of subcapsular rupture of the liver with recovery in a 9-year-old boy with an indefinite history of trauma of only moderate severity is reported.

3. The operation is described and illustrated. In the emergency a portion of the right rectus muscle was excised and packed into the liver cavity, and the omentum was brought up and packed over the muscle.

4. Anemia and shock were combated by repeated transfusions.

5. Hemorrhage was controlled by the operation itself, by transfusion, and by the administration of snake venom and klotogen.

6. Convalescence was complicated by a right pyohemothorax and localized abdominal infection. The predominating organism is both the pleural and the abdominal fluid was a hemolytic streptococcus. Sepsis was treated by drainage of the pleural and abdominal cavities and by the administration of neoprontosil.

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THE INTRAPERITONEAL USE OF HYPERTONIC GLUCOSE SOLUTION

AN EXPERIMENTAL STUDY WITH REFERENCE TO THE PREVENTION OF ADHESIONS

H. P. TOTTEN, M.D., LOS ANGELES, CALIF.

(From the Department of Surgery of the University of Southern California)

THIS paper presents the results of an experimental study undertaken to determine the value of hypertonic glucose solution in preventing the formation and re-formation of experimentally produced adhesions.

A brief review of the pertinent experimental work with intraperitoneal hypertonic glucose solution will be given, although reports from the literature are somewhat confusing because of conflicting opinions.

Following the work of Wegner, who injected liquids of a high diosmotic equivalent into the peritoneal cavity, Kuhn in 1911, repeating these experiments, suggested the use of hypertonic glucose solution in the treatment of peritonitis. He believed intraperitoneal drainage might be improved because of the fibrinolytic action of sugar. Reschke, in 1921, in a study on the effect of hypertonic solutions upon peritoneal resorption, believed the chief value of glucose in peritonitis was the delay in resorption of the exudate and was unable to confirm the fibrinolytic action suggested by Kuhn.

Pope (1914), in an experimental study on the prevention of peritoneal adhesions, chiefly concerned with the use of citrate solutions, which he reported upon favorably, found that 50 per cent sugar solution would not prevent the formation of peritoneal adhesions induced by mechanical trauma.

David and Sparks found that, while a plastic peritonitis markedly diminishes the passage of diphtheria toxin from the peritoneum, an intraperitoneal transudate, such as is produced by 50 per cent glucose solution, facilitates the passage of this toxin from the peritoneum.

Narat, experimenting with rabbits, found that it was possible to save animals from a lethal peritonitis (induced by injecting intraperitoneally a culture of staphylococci in which control animals died after from twenty-four to forty-eight hours) by injecting 20 per cent glucose from four to twenty-four hours after inoculation. He repeated the glucose injections from three to six times at intervals of six to twelve hours. Of 20 control animals, all died, while 14 of 27 animals receiving glucose survived.

Buehbinder found that by repeated intraperitoneal injections of 20 per cent glucose solution at intervals of ten to twelve hours encapsulation of drains could be prevented and their patency maintained for a period of several days. By the use of sufficient hypertonic dextrose solution, a transudate was produced which prevented fibrin formation. He also produced a chemical peritonitis by painting tincture of iodine

on the small bowel and was able to prevent adhesions in a series of 7 animals, except for an occasional strand of fibrin. He did not state the amount of glucose used nor did he test its value in preventing the re-formation of adhesions. He suggested that the method might be used to prolong drainage in case of diffuse peritonitis.

In a later study Buchbinder and co-workers studied the effect of hypertonic dextrose solution upon diffuse peritonitis. They used for a lethal standard a twenty-inch open loop of ileum. With this standard control, 28 of 31 animals died from generalized peritonitis. The average duration of the disease was four days. In those in which repeated injections of dextrose solution were given twenty-four hours following production of the open loop, the average duration of life was 1.75 days in one series and 2.2 days in another. In the latter group hypodermoclysis was given to avert dehydration. They concluded that a transudate produced by the intraperitoneal injection of hypertonic dextrose solution added to an inflammatory exudate in peritonitis produced a more rapid spread of the infection.

Morton, in an interesting study, found that local peritoneal immunity against the hemolytic streptococcus was adequately established in a large majority of animals sixty hours after the initial injection and in 100 per cent after several days by the use of nonspecific immunizing substances which included 20 per cent glucose solution. He found that the immunity was apparently dependent upon or associated with the presence of macrophages.

In the present work rabbits were used exclusively as the experimental animal. It was found that 20 per cent glucose in normal salt solution is well tolerated in the normal peritoneal cavity. By giving an equal amount of normal salt solution subcutaneously, in order to obviate dehydration, as much as 30 to 35 c.c. per pound of body weight was tolerated without apparent ill effect. Tolerance beyond this limit was not tested.

Due to the fact that this solution is hypertonic, having a high diosmotic equivalent, a transudate rapidly forms. Using 50 c.c. of the solution intraperitoneally with 50 c.c. normal salt solution subcutaneously in a series of animals, the following amount of transudate was obtained from the peritoneal cavity at the designated time interval.

The operative work was performed under intraperitoneal nembutal anesthesia, using 0.2 c.c. veterinary nembutal solution per pound of body weight. In some cases slightly more was required. This anesthetic was found quite satisfactory if the precaution was taken to withhold food for twenty-four hours prior to its use.

Strict surgical aseptic technique was maintained throughout the operative procedure. The abdomen was shaved and prepared with tincture of iodine. A right paramedian incision was used. Closure of the abdomen was accomplished with linen suture.

The method used to produce adhesions was a combination of mechanical and chemical trauma which consisted of scraping the anti-

TABLE 1

| TIME INTERVAL | AMOUNT OF TRANSUDATE |
|-----------------|----------------------|
| 1 hr., 25 min. | 127 c.c. |
| 2 hr., 5 min. | 95 c.c. |
| 3 hr., 20 min. | 79 c.c. |
| 4 hr. | 110 c.c. |
| 5 hr. | 125 c.c. |
| 6 hr., 25 min. | 146 c.c. |
| 8 hr. | 137 c.c. |
| 10 hr. | 121 c.c. |
| 15 hr., 55 min. | 2 c.c. |
| 24 hr. | 0 c.c. |

mesenteric portion of the small intestine with a knife blade until the serosa was abraded, followed by the application of tincture of iodine. This method was essentially the one used by Ochsner and Garside in their experimental work with papain except that they used gauze to abrade the serosal surface. I found, however, that in the rabbit the intestine adhered to the gauze so that there was danger of tearing through the entire bowel wall or mesentery; whereas, when the knife blade was used, the serosal surface could be abraded safely and satisfactorily.

RESULTS

In a series of 16 animals (Group I) adhesions were produced in every instance, reoperation being performed one to five weeks later. In a second series of 16 animals (Group II) from 10 to 15 c.c. of 20 per cent dextrose in normal salt solution per pound of body weight was introduced intraperitoneally following intestinal trauma just before completing closure of the peritoneum. In this group there were 14 cases in which adhesions did not form. Of the 2 in which adhesions formed, 1 was complicated by wound infection and intraperitoneal abscess and the other showed adhesions of limited extent (2 cm.) between intestine and mesentery but not between intestinal coils. In 12 animals in Group II in which the introduction of glucose solution at the time of trauma prevented the formation of adhesions, trauma at reoperation without the introduction of glucose produced adhesions in 100 per cent of the cases.

Finally at reoperation in 11 cases of Group I, adhesions were separated and the glucose solution was introduced with the result that adhesions did not re-form in 7 cases (67 per cent).

Six additional animals were used which were not included in the results for the following reason: 2 animals died as a result of too much anesthetic, 2 from excessive trauma, in one case due to peritonitis from perforation of the intestine and in the other from gangrene of the bowel; 1 died from bowel strangulation due to intussusception at the site of trauma and 1 from abdominal wall abscess followed by evisceration.

Although not the primary purpose of this study, it was deemed advisable to observe the effect of this solution upon the survival of the animals in the presence of peritoneal infection.

An attempt was made to establish a satisfactory lethal standard that would simulate human peritonitis.

Ligation of the fecal-filled appendix was performed on 12 animals, but it was found that the results were inconstant due to variation in the size of the appendix and inability in some instances to squeeze successfully enough intestinal content into the appendix to distend it. Death rapidly ensued if perforation occurred. However, if perforation did not occur, which condition obtained in 7 instances, the animal survived though the appendix became greatly distended and there developed local peritonitis and abscess.



Fig. 1.—Photograph of control rabbit sacrificed seven days after mechanical and chemical trauma to small intestine. A fibrinous exudate has formed between loops of the traumatized intestine. The small intestinal loops are dilated, showing evidence of a moderate ileus.

A satisfactory lethal standard was found to be a 10 c.c. suspension of 0.15 Gm. fecal material. Death occurred within twenty-four to forty-eight hours in 10 consecutive control animals.

In the next 10 animals 20 c.c. of 20 per cent glucose in normal salt solution was injected intraperitoneally seventy-two, forty-eight and twenty-four hours before intraperitoneal inoculation of fecal material. The result was 7 recoveries and 3 deaths. Death occurred in the fatal cases from three to four days after inoculation.

In another group of 5 animals the glucose solution was introduced intraperitoneally at the time of inoculation. The result was death within a period of sixteen to twenty-four hours in every case. In the

latter group there was little evidence of peritoneal reaction or fibrin formation as contrasted with the preceding group, in which signs of well-marked peritonitis were present.

Those cases prepared preoperatively with glucose solution which survived were autopsied from two to four weeks later.

The character and extent of the adhesion indicated that these animals had survived a widespread peritonitis. In 2 cases there were residual abscesses.

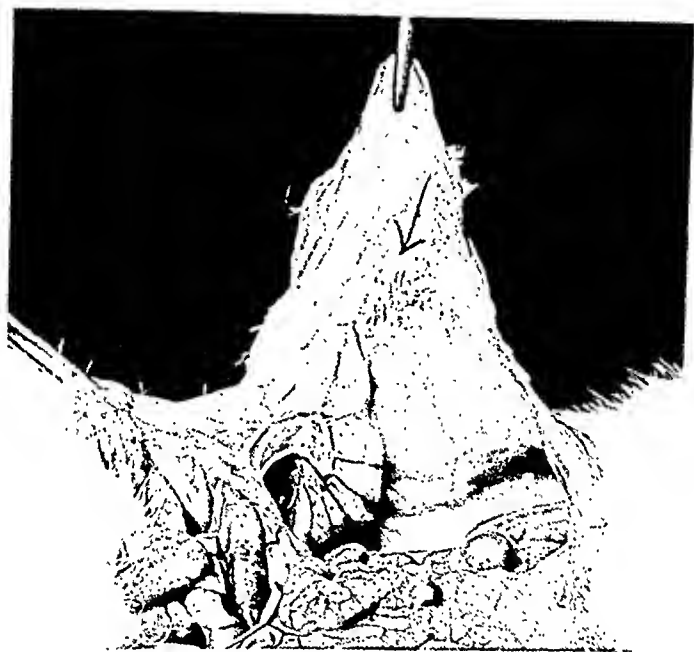


Fig. 2.—Photograph of control rabbit sacrificed two weeks after mechanical and chemical trauma to small intestine. Dense adhesions have formed between loops of traumatized intestine and between intestine and anterior parietal peritoneum. Arrow indicates area where adherent bowel was stripped from parietal peritoneum.

It seems evident, in the light of Buchbinder's observation as well as the results of the present work, that the introduction of this solution in the presence of peritonitis or coincident with peritoneal contamination increases the rate of absorption from the peritoneum and interferes with the development of the natural peritoneal defense mechanism. This is apparently due to two factors: diffusion of the infectious material over a wider area of peritoneal surface and interference with the formation of fibrin. On the other hand, the results obtained in this study confirm the work of Morton who found that, if given time, the irritating effect of hypertonic glucose solution in bringing forth a transudate apparently acts as a nonspecific immunizing agent. Thus, provided complete absorption of the transudate has taken place prior to gross peritoneal contamination, it tends to combat the lethal effect of peritonitis.

While no attempt was made to study, in detail, the intra- and extra-peritoneal cellular response, omental sections were taken from control and prepared animals. Both showed the presence of a very acute inflammatory process. However, the control specimens, grossly, showed less injection of the blood vessels. On microscopic examination the controls showed fewer infiltrating cells and these consisted largely of polymorphonuclear leucocytes. Sections from prepared animals showed considerably larger areas of infiltration and a more mixed type of cellular infiltrate, with more evidence of phagocytosis.



Fig. 3.—Photograph of rabbit sacrificed seven days after mechanical and chemical trauma to small intestine; 20 per cent glucose in normal salt solution was introduced intraperitoneally following trauma. There is no evidence of peritoneal adhesions. Evidence of inflammatory reaction of the peritoneum is minimal.

In evaluating experimentally the efficacy of a particular solution in preventing the formation of adhesions, the factor of infection must be taken into consideration. When chemical and mechanical trauma is used to induce the formation of adhesions, such trauma may devitalize the intestinal wall sufficiently to allow penetration of bacteria, and bacterial peritonitis develops and is added to the already existing peritonitis of chemical and mechanical origin. This bacterial trauma continues to act for a period of several days and by virtue of its prolonged action tends to nullify the effect of the adhesion-preventing solution.

It is quite possible, when glucose is used immediately following mechanical and chemical trauma, if such trauma is not extreme, that an additional beneficial factor comes into play: the nonspecific immunizing effect of the solution prevents the development of bacterial peritonitis, provided the bacterial invasion is limited, which otherwise would develop incident to chemical and mechanical insult and is thus effective in preventing the formation of adhesions. However, when trauma is extreme, for example, tearing the bowel wall in separating adhesions, bacterial peritonitis will follow, irrespective of the use of the solution, and adhesions will form. It was observed that those animals that had received the solution following trauma reacted better, were more alert, were able to eat sooner, and retained their preoperative weight more consistently than the animals in the control series. Aside from the effects of adhesions in producing various grades of intestinal obstruction, it is believed that the more severe postoperative course of the control animals during the first several days was due essentially in some cases to a peritonitis of bacterial origin.

COMMENT

Hypertonic glucose in normal salt solution was selected for use in this study because the transudate which develops upon its introduction into the peritoneal cavity occurs consistently. By virtue of this large transudate, which is fibrin free, mechanical isolation of intestinal coils acts to prevent the formation of adhesions between contiguous loops of bowel.

This solution, in the absence of intraperitoneal infection, is entirely innocuous except for the possible danger of dehydration, and then only if it is used in excessive amounts. Dehydration, however, may be easily controlled. It has an advantage over most solutions because of the fact that its sugar and salt content may be utilized.

Peritoneal adhesions which consistently occur following a combination of mechanical and chemical trauma may be prevented from forming in the great majority of instances by the introduction of 20 per cent glucose in normal salt solution at the time the trauma is induced. Adhesions may be prevented from re-forming after separation in the majority of cases if the solution is introduced into the peritoneal cavity at the time the adhesions are separated, provided the trauma incident to separation of the adhesions is not so great as to produce infection within the peritoneal cavity, such infection being an adhesion-producing factor which continues to act for a period of time longer than the transudate (adhesion-preventing factor) remains within the peritoneal cavity.

It is believed the percentage of adhesion-free cases in Group II would have approximated 100 per cent if infection had not occurred in the two cases that showed adhesions. It was the definite cause in one and the probable cause in the other.

In Group IV there were several cases in which the adhesions were so dense that great difficulty was encountered in separating them satisfac-

torily and in three instances tearing of the bowel wall occurred, which it is believed tended to offset the effect of the transudate by virtue of the excessive trauma.

TABLE II

| | GROUP I | GROUP II | GROUP III | GROUP IV |
|-------------------------|--|--|---|--|
| | Bowel scraped and tincture of iodine applied | Bowel scraped, tincture of iodine applied and 20 per cent glucose in normal salt solution introduced intraperitoneally | Bowel scraped and tincture of iodine applied at reoperation in Group II | Adhesions separated at reoperation in Group I and 20 per cent glucose in normal salt solution introduced intraperitoneally |
| Number of animals | 16 | 16 | 12 | 11 |
| Percentage of adhesions | 100 | 13.5 | 100 | 36.4 |
| Grade of adhesions* | (IV) 12 (III) 2 (II) 1 (I) 0 | 0 0 1 1 | 9 2 1 0 | 0 1 2 1 |
| Without adhesions | 0 | 14 | 0 | 7 |

*IV, Dense to moderately firm adhesions over most or all of traumatized area; III, moderately firm adhesions over most of traumatized area; II, moderately firm to easily separated adhesions of limited extent; I, easily separated adhesions of limited extent.

SUMMARY AND CONCLUSIONS

1. Hypertonic glucose in normal salt solution, aside from possible effects of dehydration when used in excessive amounts, is entirely innocuous when placed within the normal noninfected peritoneal cavity.

2. A large transudate forms which is completely absorbed within a period of twenty-four hours.

3. This solution, when used intraperitoneally, possesses value in preventing the formation and re-formation of experimentally produced adhesions.

4. It apparently confers a certain degree of nonspecific immunity upon the peritoneum.

5. In the presence of gross peritoneal contamination the use of this solution, interfering with fibrin formation, hastens the spread of infection.

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Peritoneal adhesions which consistently occur following a combination of mechanical and chemical trauma may be prevented from forming in the great majority of instances by the introduction of 20 per cent glucose in normal salt solution at the time the trauma is induced. Adhesions may be prevented from re-forming after separation in the majority of cases if the solution is introduced into the peritoneal cavity at the time the adhesions are separated, provided the trauma incident to separation of the adhesions is not so great as to produce infection within the peritoneal cavity, such infection being an adhesion-producing factor which continues to act for a period of time longer than the transudate (adhesion-preventing factor) remains within the peritoneal cavity.

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In Group IV there were several cases in which the adhesions were so dense that great difficulty was encountered in separating them satisfac-

patients were very happy that they could use their hands at once when they put on this apparatus. One of its advantages is also that it can be washed or changed without much expense, and therefore kept constantly clean and hygienic.

Fig. 1.



Fig. 2.



Fig. 3.

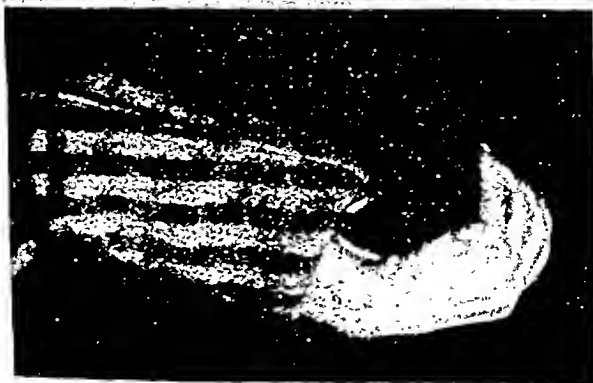


Fig. 1.—Photograph showing the position of the hands in musculospiral injury. Because of flexion of the fingers, the grasp is weak.

Fig. 2.—Extension of the finger is secured by fastening elastic to a glove which is attached to the shirt or coat, correcting the malposition shown in Fig. 1.

Fig. 3.—In the hyperextended position of the wrist and finger, it is possible to grasp tightly, thus overcoming any weakness occasioned by the position shown in Fig. 1.

SIMPLE APPARATUS FOR THE RELIEF OF SOME PALSIES OF THE UPPER EXTREMITIES

PROF. DR. EUGENE PÓLYA, BUDAPEST, HUNGARY

I. WRIST DROP

ONE of the most disagreeable consequences of the palsy of the radial nerve is the loss of power of the digital flexors. They are not paralyzed, but still the patient is unable to produce their powerful contraction; he cannot grasp with them strongly enough, and cannot hold any object securely. The reason is clear. The palsy of the antagonists brings about the shortening of the digital flexors, and hereby the amplitude of their movements is greatly reduced. One can grasp something powerfully enough only if the movement of flexion begins when the fingers are well extended. If at the beginning of the grasping movement the fingers are already in a flexed position (as they always are when musculospiral nerve is paralyzed), the grasp will be weak (Fig. 1). If the palsy of the radial nerve is of longer standing, the inactivity leads to atrophy not only of the extensors, but also of the flexors of the finger, and this condition may be aggravated by the loss of the memory of the motor functions of the palsied hand (Oppenheim).

Therefore, it is important that in the treatment of radial palsy the condition of the digital flexors should also be duly regarded. It is not sufficient to treat only the cause of the palsy (the mechanical or toxic injury to the nerve) and treat this adequately (for instance, cure the chronic lead poisoning, repair the wound of the nerve, etc.) and to keep the paralyzed radial nerve itself and the muscles innervated by it in as good condition as possible (electricity, massage, hot baths, etc.). One must also care for the adequate function of the antagonists, which can be done only when one secures for the flexor of the fingers a possibility for powerful contraction, and this can be done only by keeping them in an extended position which will not hinder their contraction. This will also more or less secure the usefulness of the paralyzed hand even during the duration of the palsy and it will certainly facilitate and hasten the complete restitution in cases which are likely to heal. It will prevent, of course, the development of contractures.

There are many complicated and expensive types of apparatus devised as substitutes for the failing function of the digital extensors; these are generally very uncomfortable. One can provide a very simple, cheap, and comfortable apparatus with the help of a glove and strips of garter elastic, and one need not wait days and weeks for the technician to make it. Any nurse can get it ready in a few minutes. I have used this simple apparatus for many years in many cases and found it (as others have who have used it according to my advice) most satisfactory. The

pletely useless, but it can be made useful by a broad strip of garter elastic which is sewn to the shoulder and to the dorsal and ulnar side of the wrist of a bedjacket, blouse, or suit-coat sleeve which keeps the elbow bent at an angle of 45 degrees and the hand at about the level of the mouth. The function of the triceps muscle being normal, this permits the patient to keep his hand in any position between 45 and 180 degrees. This simple apparatus (Fig. 4) was constructed for a girl who contracted palsy of the Erb type after an operation. She was able with this apparatus to touch her mouth, her hair, and her face with her hands so that she could wash and comb her hair herself and use both hands when eating. She was a poor girl who lived alone and had to do all the work in her house, and she could do this perfectly with the help of her apparatus. She recovered from her palsy, but, until this happened, the apparatus made her perfectly able to care for herself.

One takes a glove, preferably one of thin leather or tough cotton which does not tear easily, and fastens a strip of garter elastic all along the dorsal aspect of each of its fingers. These strips are fastened by sewing them tightly to the fingers of the glove from the region of the nails to the region of the metacarpophalangeal articulations. Then one sews the strips together, beginning in the region of the wrist, forming a common band which is then fastened with a safety pin somewhat above the middle of the forearm to the shirt sleeve (Fig. 2). It is good to bandage the shirt sleeve to the forearm tightly with a few turns of bandage in order to avoid its slipping; that is, its being pulled down by the elastic. In the illustrations the band is shown fastened to the



Fig. 4.—Position maintained by simple bandage consisting of the use of elastic bands sutured to the shoulder and to the ulnar and dorsal sides of the wrist of a jacket or blouse. In this way patients with Erb paralysis can touch the mouth, hair, and face with the involved hand.

sleeve of a dark coat to show the white elastic more distinctly, but it is surer to fix the elastic in the above-described way to the shirt sleeve and it is also less conspicuous. As Fig. 2 shows, the garter elastic keeps the wrist and the fingers constantly in a somewhat hyperextended position and in this manner promotes the powerful contraction of the digital flexor muscles and a firm grasp (Fig. 3).

II. ERB'S PALSY

The most prominent and constant feature is palsy of the shoulder and the flexors of the elbow; whereas, the extension of the forearm as well as all the movements of the fingers are normal. Such an arm is com-

RADIATION THERAPY FOR RECURRENT SACROCOCCYGEAL CYSTS AND SINUSES*

ROBERT TURELL, M.D., NEW YORK, N. Y.

THE NUMEROUS studies on sacrocoecygeal cysts and sinuses to date have been unproductive of unanimity of opinion as to the essential aspects of this lesion. The wide diversity of opinion regarding the etiology and genesis is responsible for the lack of understanding of this lesion.

Most investigators agree that the sacrocoecygeal lesion is congenital in origin and that it arises from the ectoderm. They disagree, however, as to whether nerve tissue or integument is the source of origin. For the sake of brevity we shall limit this discussion to the recent work of the two proponents of these opposite theories. Gage¹ has presented excellent evidence to show that sacrocoecygeal cysts and sinuses arise from the caudal end of the medullary canal. He stated that in rare cases the sinus may extend into the sacrocoecygeal joints, sacral canal, or to the dura and thus communicate with the subarachnoid space or cord. Instances of meningitis originating from infected sacrocoecygeal cysts, as well as the escape of cerebrospinal fluid from the sacrocoecygeal lesion, have been reported. Gage furthermore showed the presence of nerve tissue and a persistent absence of sebaceous cysts in the depth of excised specimens.

Fox,² on the other hand, presented embryologic proof to show that the invagination of normal ectoderm is the cause of sacrocoecygeal cysts and sinuses. Gage³ in a recent critique of Fox's work stated that the latter "described the development of the median raphe." In passing, it should be noted that Stone⁴ considers the sacrocoecygeal cyst as an analogue of the preen gland of birds. The preen gland embryologically and functionally resembles the mammary gland of the higher vertebrates.

In the final analysis, it is acute or chronic infection which heralds the presence of the lesion to the patient and to the surgeon. Both judge the success or failure of the surgical treatment by the incidence of recurrence. Most surgeons believe that the important causes of recurrence are the failure of removal of the primary infected scar tissue and eradication of the infection. All branches of the sinus as well as ectopic epithelium should be removed during the original operation. Obliteration of dead space is another important factor.

It is generally conceded that the published reports on recurrence do not represent a fair cross section of the work done throughout the country. The unreported unsuccessful results do not necessarily reflect the

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ETHYL CHLORIDE SPRAY FOR SPRAINED ANKLES*

LEWIS COZEN, M.D., AND
BENJAMIN S. HOLLOMBE, M.D., LOS ANGELES, CALIF.

CREER in 1939 mentioned the use of ethyl chloride spray locally in sprained ankles. Novocain injection had been reported previously as giving instantaneous and permanent relief. Apparently, both the novocain and the ethyl chloride spray "break up" the vasomotor paralysis, which is in no small part the cause of the pain as well as the local swelling.

The technique of using the spray is quite simple. The area of tenderness, generally in the region of the sinus tarsi, is localized as accurately as possible. This area is sprayed with ethyl chloride until the area is white. The patient is then allowed to walk off with no strapping or bandaging of any kind. If the pain has not disappeared, the usual adhesive strapping may be applied.

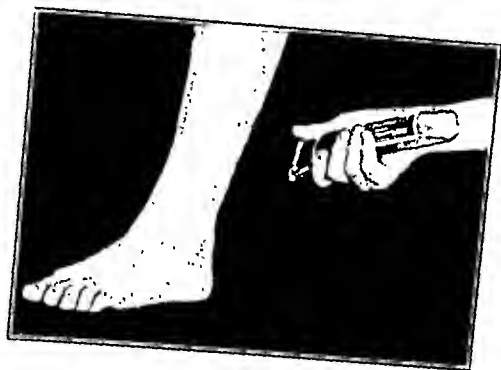


Fig. 1.

The spray has been used in eight cases with satisfactory results. It may be of aid in eliminating the persistent swelling and pain in old ankle sprains. One of the eight patients treated first was seen two weeks after injury. The ethyl chloride spray was applied twice with a seven-day interval between the two applications. Diathermy, contrast baths, and an ice bandage had been of no avail in relieving the pain and swelling prior to the use of the ethyl chloride.

Ethyl chloride spray will be used in the future in patients complaining of swelling and localized pain in the ankle accompanying healed fractures of the ankle and foot. Whether the cause of the swelling and pain in such cases is an actual thrombophlebitis, as Homans postulates, there is little doubt that vasomotor paralysis plays an important part. Ethyl chloride spray may prove to be of value in selected cases of swelling and localized pains affecting the ankle region.

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*Since this paper was written, ethyl chloride spray has been used by the authors as an aid in the treatment of a number of orthopedic affections. An article on this subject is to be published in the near future.

CASE REPORTS

CASE 1.—A. S., a 37-year-old man, was seen on March 30, 1938, because of irritation in the perineum of one year's duration, and purulent discharge from a recurrent sacrococcygeal sinus. The past history included a carbuncle of the neck which occurred six years before and was controlled by radiation therapy, and an excision of the sacrococcygeal cyst two years before which remained healed for about two months. Since then he has had a continuous discharge from the operative wound. Examination was normal throughout except for the presence of an induration and reddening of the perineum with a small carbuncle on the left side, 3 cm. from the anal orifice, and a recurrent sacrococcygeal sinus with three openings in the scar. The sinus measured about 5 cm. in length and extended cephalad. It was felt that purulent discharge from the sacrococcygeal sinus caused the cutaneous perineal lesion. The possibility of osteomyelitis of the coccyx was entertained but could not be ruled out definitely. After failure to effect improvement through better hygiene and topical medication, radiation therapy was decided upon. A total of 675 r. (125 kv. unfiltered) was given to the perineum and the sacrococcygeal area over a period of two months. The sacrococcygeal sinus closed shortly before the cessation of treatment and remained closed for about five months when the patient disappeared.

CASE 2.—R. A., a 24-year-old man, was seen on May 4, 1938, because of persistent purulent discharge from a recurrent sacrococcygeal sinus which was associated with moderate pain. Excision of a sacrococcygeal cyst had been performed about fourteen months before. The physical examination was normal except for an opening in the sacrococcygeal area 1 cm. in diameter, with excoriation of the posterior perianal skin. He was given radiation therapy, 650 r., over a period of six weeks. The sinus has remained closed to date. The scar appears to be softer in quality and more bluish in coloration than those commonly observed elsewhere. There has been no pain since the closure of the sinus.

DISCUSSION

The first case herein reported is of special interest. The concomitant cutaneous lesions in the perineum did not respond to simple topical treatment. Therefore, radiation therapy to the perineal and sacrococcygeal lesions was given a trial. After a lapse of eight weeks, during which time 675 r. of unfiltered radiation therapy were given by a dermatologist, the perineal cutaneous lesion showed marked improvement, and the sacrococcygeal sinus closed. Lack of prolonged follow-up studies makes it impossible to state the final outcome in this instance. The foregoing observation, however, led to further clinical investigation, and to this presentation.

Because of the gradual improvement observed during the course of radiation therapy in the first instance, another patient with a recurrent infected sacrococcygeal sinus (Case 2) was subjected to similar therapy. After the administration of the 250 r., there was cessation of the purulent discharge.

Two additional cases of recurring, infected sacrococcygeal sinus were subjected to radiation therapy. One case received a total of 825 r. The remaining cases required less than 700 r. The wounds all healed within

caliber of work of the good surgeon. By the same token, excellent results are not always obtained in the hands of the average surgeon. To evaluate the present status of this problem, Kleekner,⁵ by means of a questionnaire sent to the leading proctologists of the United States, attempted a statistical study to show their experience with the choice of operation and the incidence of recurrence of the lesion. He found that there were recurrences in 48 instances (1.13 per cent) in 4,231 cases where excision and packing had been done. This is indeed a very excellent record. Rogers and Dwight,⁶ utilizing excision with cautery and packing, reported only 2 failures in a series of 140 consecutive, unselected, new and recurrent cases. In spite of their meticulous postoperative care, they encountered complications including abscess formation in 6 cases. In a previous communication Rogers⁷ reported a recurrence of 30 per cent in the traced cases following radical block resection with packing. McKirdie⁸ reported a series of 87 patients who were operated upon by 24 different surgeons at the teaching hospital of the University of Iowa Medical School. Sixty-one cases were followed. He found a recurrence in 7 out of 11 patients (63 per cent) where wide excision with packing was employed. This operative approach was used chiefly in the treatment of recurrent cases.

Utilizing the operation of excision and primary closure of the wound, Gage³ reported 42 of his own and 54 of Strug's cases without a single recurrence. However, superficial and deep infections occurred during convalescence. Ferguson and Meera⁹ reported 3 recurrences in a series of 37 patients (8 per cent) after their modified type of excision and primary closure was done. Kleekner⁵ reported recurrences in 85 out of 365 cases (23.29 per cent) after excision and primary closure. Not all cases in this series healed by first intention; some wounds broke down but eventually healed. He also recorded a series of 103 cases of excision and primary closure, where, during convalescence, the wounds had to be opened for drainage because of infection. These wounds later healed by "open granulation." In this last group the incidence of recurrence was 4.8 per cent (5 cases). McKirdie⁸ observed 14 recurrences (31 per cent) in 45 follow-up patients in whom excision and primary closure with drainage were performed. It should be interpolated that primary closure is usually done on favorable cases. This fact notwithstanding, primary closure is sometimes followed by disastrous complications such as widespread gangrene of the wound and surrounding tissues caused by anaerobic organisms.^{10, 11}

From the foregoing it is obvious that recurrences follow almost all types of operations. There are but few and fragmentary figures dealing with recurrences following operations upon recurrent cases.

The following case histories are reported because they suggest effective treatment. It should be added that the follow-up period has been too short for the final evaluation of this method of therapy.

THE CONSERVATIVE MANAGEMENT OF SIGMOIDOSCOPIC PERFORATION

MYRON A. SALLICK, M.D., NEW YORK, N. Y.

(From the Mount Sinai Hospital, Service of Dr. John H. Garlock)

FREE intraperitoneal penetration of the rectum or sigmoid during the course of instrumental examination is always a serious accident. The occurrence of this complication, when recognized, is generally held to call for immediate laparotomy for closure of the perforation. Even when operation is performed early, the mortality rate in these cases is high. When operative treatment is attempted after an interval of several hours, the outcome has proved almost invariably fatal.¹

The grave prognosis usually attendant upon the customary surgical handling of sigmoidoscopic perforation merits the recording of a case of this type successfully treated by conservative measures. This experience, although limited to a single case, is reported in the belief that, under certain circumstances which will be defined below, expectant measures may be preferable to operative treatment.

CASE REPORT

K. K., female, aged 70 years, was admitted to the Mount Sinai Hospital on the surgical service of Dr. John H. Garlock in the afternoon of August 26, 1937 (Hosp. No. 413308).

About three hours previously, she had been sigmoidoscoped by an experienced gastroenterologist. During the course of this examination, the patient had suddenly experienced intense left lower abdominal pain accompanied by severe cramps. The physician at once suspected the possibility of rupture of the bowel, withdrew the instrument, and referred the patient for hospital admission.

Sigmoidoscopic examination had been undertaken in the attempt to determine the source of bleeding from the lower intestine which had occurred intermittently for two years. Earlier studies by barium enema and proctoscopy had been negative.

Examination.—The patient was seen on the ward shortly after her admission to the hospital. She was a small, poorly nourished, pale, rather feeble, elderly woman in moderate discomfort. Her rectal temperature was 99° F.; the blood count was 11,800 white blood cells, with 88 per cent polymorphonuclears. Her abdomen was full but not tense. Generalized tenderness was present. There was no muscular rigidity; no palpable masses could be found. There was no dullness in the flanks or fluid wave. Liver percussion was normal.

A scout abdominal x-ray film had been taken with the patient upright. This was reported to show no evidence of free intraperitoneal gas.

Course.—In view of the patient's generally poor physical state, together with the absence of definitive local signs or systemic reaction, conservative management was decided upon although it was felt that there had most likely been a visceral perforation. General supportive measures were instituted.

On the following afternoon the patient's temperature rose abruptly to 102.4°. She complained of pain in the right shoulder and an increase in lower abdominal discomfort. Distention was more marked. No flatus had been passed. Liver

a period of two months. The quality of the scar tissue in all cases appeared to be inferior to that observed in wounds elsewhere in the body.

During and after the period of radiation therapy, rigid hygiene of the infected and neighboring parts was insisted upon. To date there have been no recurrences. Should recurrences take place, a second course of radiation therapy may be considered. It is conceivable that, when all branches of the sinus or ectopic epithelium are incompletely removed during the original operation, radiation therapy may fail, and reoperation may become necessary.

For the preparation of this article a perusal of the literature was made and only one paper dealing with radiation therapy in this condition was found. Smith¹² used radiation therapy in two cases postoperatively with good results. Our technique of administration was essentially the same as that used by him, but our dosages were larger.

SUMMARY

1. Radiation therapy is advocated as a substitute for operation for the recurrence of infected sacrococcygeal sinus. Illustrative case reports are given.

2. Reoperation may be indicated in cases where branches of the sacrococcygeal sinuses or ectopic epithelium were incompletely removed at the original operation.

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ment was noted. Flatus had been passed per rectum spontaneously. The temperature was at a lower level. The abdomen was somewhat softer, although distention and tenderness persisted. On September 1, the sixth hospital day, the bowels moved, with the evacuation of a large amount of fresh fluid blood and a huge clot. By rectal examination, a broad area of pelvic induration was found. Rectal bleeding continued on the following day. The hemoglobin fell to 50 per cent. Transfusions of citrated blood were given on September 1, 4, and 6. From then on gradual improvement continued. The patient was discharged home on Sept. 12, 1937, seventeen days after her admission to the hospital. The pelvic mass was diminishing in size but was still firm. The patient was afebrile.

Subsequent roentgenologic examination by barium enema failed to show any definite evidence of organic lesion in the sigmoid colon. The patient was last heard from on March 18, 1939, about one and one-half years after leaving the hospital. She then felt well and was doing her own housework, but still had occasional rectal bleeding which had not been further investigated.

COMMENT

Even in the most skillful hands, perforation during proctoscopy and sigmoidoscopy can and does occasionally occur. It is an unfortunate commentary on the status of medical recording that these accidents go practically unmentioned. Reports of traumatic rupture of the lower colon from other causes are numerous. Instances of impalement, compressed air blowouts, and foreign body and enema tip penetrations are frequently cited. Yet thorough search disclosed only two case reports in the American literature dealing directly with proctoscopic perforation.^{2, 3} Of these cases, one, in which laparotomy was done, resulted fatally, and the other, treated expectantly, recovered. Another patient with this complication, in England, failed to survive operative treatment.⁴ In the foreign language journals, also, case reports of this complication are infrequent.^{5, 6}

The most comprehensive article on this subject is by Crohn and Rosenhak,¹ who collected, among other types of traumas arising out of sigmoidal manipulation, thirty-nine cases of rupture resulting from sigmoidoscopy. These cases were compiled from the literature and personal observations, but chiefly by questionnaire. In tabulating results, these authors did not differentiate between sigmoidoscopic perforation and that due to therapeutic and other diagnostic procedures. Their findings indicate a mortality of about 50 per cent, even with immediate operation. Of the patients operated upon seven or more hours after perforation, there was not a single recovery in five cases.

There were four cases of sigmoidoscopic perforation treated on the ward services of the Mount Sinai Hospital during the years 1933 through 1938. Of these patients three were admitted to the hospital with this complication, and there was one instance in which the accident occurred to a patient already in the hospital. Operation was carried out in three cases, with one death and two recoveries. One patient, whose case history is given above, was treated successfully without operation. It is

dullness was now obliterated. Local tenderness was greater, and rebound tenderness was present over both lower abdominal quadrants.

Roentgenologic examination at this time showed a large collection of free gas below the right leaf of the diaphragm and a smaller amount on the left side. (Fig. 1.)



Fig. 1.

With the definite establishment of the diagnosis of visceral perforation and in the face of signs of increasing peritoneal irritation, the advisability of surgical intervention was again considered. The case was discussed by the staff, and it was agreed that operation should be withheld. The following reasons were held to justify this decision: The patient was a poor surgical and anesthetic risk. It might prove difficult to locate the perforation and to close it, particularly if a neoplasm were present, necessitating a prolonged operation. Since more than twenty-four hours had already elapsed after the accident, the likelihood of benefit from operation seemed small. The natural defenses of the peritoneum to the spread of infection would be disturbed by the manipulation. It was felt that, with continued conservative and supportive measures, the patient might localize the infection.

Accordingly, the method of treatment was not altered. The next morning, the patient seemed slightly better. On the third day after admission, definite improve-

tract, the administration of parenteral fluids, and, in some instances, repeated blood transfusions. Close observation is essential so that complications such as hemorrhage and the development of localized abscesses may be promptly recognized and cared for efficiently. Essentially this means that accidents arising out of sigmoidoscopy should be individualized and not treated routinely. Only in this way can the present poor results be improved.

CONCLUSIONS

1. Perforation of the bowel during sigmoidoscopic examination need not necessarily call for immediate abdominal exploration.

2. The mortality rate in cases operated upon for this complication is high.

3. The fact that the lower colon has usually been thoroughly cleansed prior to the examination makes gross contamination of the abdominal cavity unlikely.

4. The ability of the peritoneum to take care of infection that is not overwhelming deserves consideration.

5. Recovery can occur through the employment of expectant and supportive measures alone.

6. In aged and poor-risk patients with sigmoidoscopic perforation and in cases where there has been a delay of several hours in establishing the diagnosis or in instituting treatment, conservative rather than operative management is suggested.

Acknowledgment is made to Dr. H. Neuhof, Dr. R. Colp, and Dr. A. Hyman for the privilege of including, in this report, a case from each of their respective services.

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significant that in each of the patients operated upon, although the perforation was into the free abdominal cavity, no gross peritoneal spilling of bowel content was found. The laceration in each instance was small, not readily exposed, and its closure was technically difficult.

DISCUSSION

The patient who is the subject of the present report experienced a perforation of the lower colon into the free abdominal cavity while undergoing a sigmoidoscopic examination. The condition was promptly recognized by the attending physician, and she was referred to the hospital without delay. Because of the patient's advanced age and generally poor physical condition, treatment was restricted to conservative measures and operation was not undertaken even though the diagnosis of viscerol laceration was proved. The satisfactory outcome with prompt recovery, in this case, serves to support the value of nonoperative management of this complication, particularly in view of the high mortality rate reported when active surgical measures have been employed.

The relative cleanliness of the empty lower bowel in patients who have been prepared for instrumental examination by enemas and irrigation and the well-known capacity of the peritoneum, especially in the pelvis, to effectively combat or localize infection that is not overwhelming should be considered by surgeons who are faced with this problem. The sigmoidoscope, due to its size, lacerates the colon without actually penetrating into the abdominal cavity. The tear usually takes place anteriorly at or near the rectosigmoidal junction, a location where the sigmoid and small intestine can fall across the opening and serve to wall it off. These factors tend to result in the formation of a limited rather than a disseminated infection. Operative manipulation may disturb rather than assist this favorable defensive setup. Considering the indifferent success experienced with operative treatment, the peritoneum, at least in patients of poor risk, deserves a chance to fight its own battle without interference.

The foregoing is not intended to infer that operation be withheld in all cases of sigmoidoscopic perforation. When the diagnosis has been made early and the patient is otherwise in good condition, it is agreed that laparotomy is advisable. Conservative treatment is to be reserved for the elderly and poor-risk patients and for cases in which, for one reason or another, there has ensued a delay of several hours either in establishing the diagnosis of perforation or in instituting treatment. In such instances, it is felt that a successful outcome is more likely to follow from conservative measures than with surgical intervention. It is also well, perhaps, to stress the point that conservative management is not meant to be synonymous with "careful neglect." These patients require active employment of all the measures called for in the Ochsner treatment of peritonitis: hospitalization, opiates, rest of the alimentary

parietal, 2; and temporal, 2. The locations of tumors producing down-and-back shift were: frontal, 4; frontotemporal, 1; temporal, 1; frontotemporoparietal, 1; and pituitary adenoma, 1. The location of the one tumor producing an upshift was in the sella turcica, a pituitary adenoma.

It is instantly apparent that any aid in the localization of brain tumors which is roughly dependent upon a postadolescent age in the subject is valueless in that large group of tumors occurring in adolescence and preadolescence. Furthermore, either from a priori reasoning or from the data presented, there appears to be little hope of assistance in those tumors which lie below the tentorium cerebelli. However, a priori reasoning might lead one to expect assistance in the localization of supratentorial tumors. From the data presented, however, it seems that this is only true in lateralizing the tumor, a feat sometimes difficult but more often quite sure. Unfortunately, here again we must subtract from the value of the pineal shift since in the anteroposterior views the calcified gland is viewed in its narrowest diameters and positive identification is further made difficult by overlying shadows of frontal sinuses and their trabeculae. Also in 2 of the 14 cases herein presented the shift was actually toward the side of the lesion. Regardless of the location of the tumor, pineal shift in the lateral roentgenogram is almost always back, down, or both. The reason for this fact is not immediately apparent, but it is supposed that the stereotyped shift is a function of the semirigid crescentic falx cerebri which must direct any expanding force on either side of it downward and backward in the direction of the most free space.

Concerning the type of tumor most likely to produce pineal shift, little can be said from these data other than that the gliomas, the most frequent type of tumor, are closely followed by the meningiomas.

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A NOTE ON THE RELIABILITY OF ROENTGENOGRAPHICALLY DETERMINED PINEAL GLAND SHIFT IN BRAIN TUMORS*

R. YORKE HERREN, M.D., PH.D., PORTLAND, ORE.

RECENT articles¹⁻³ on the roentgenographic displacement of calcified pineal shadows place an apparent valuable aid in the hands of one who wishes more sharply to localize intracranial neoplasms. To test the validity of this aid, 194 cases of microscopically proved primary brain tumor were arbitrarily selected. Among this number there were 80 cases with calcification identifiable in the pineal gland in either the lateral or anteroposterior view. Eleven of these were purely subtentorial and 68 purely supratentorial in location. One case was a papilloma of the choroid plexus of the lateral ventricle which seeded to the cerebellum and so was both supra- and subtentorial in location.

In this report the designation of normal or abnormal positions of the pineal shadows is in accordance with either the method of Vastine and Kinney⁴ or the proportional method of Fry.^{2, 3}

Of the 11 subtentorial tumors with calcified pineal glands, only 2 produced a displacement of the gland from its normal position. One case, a posterior fossa meningioma, showed a lateral shift as viewed in the anteroposterior films; and the other, a cholesteatoma, showed an upward and forward shift. The one case which seeded to the posterior fossa showed no displacement of the calcified gland.

Of the 68 supratentorial tumors, 31 produced a displacement of the calcified gland from its normal position. Six of these cases displayed a shift in the lateral as well as the anteroposterior view. So in this material there are 21 instances of abnormal position of the gland in the lateral views and 16 instances of abnormal position of the gland in the anteroposterior views. In 14 of the 16 instances of pineal shift in the anteroposterior views, the shift was away from the side of the tumor and in 2 instances the shift was toward the side of the tumor. In the 21 instances of pineal shift in the lateral views, the direction of shift was down in 5 cases, back in 8 cases, down and back in 7 cases, and up in 1 case.

The locations of tumors producing downshift were: frontal, 3; third ventricle, 1; and intralateral ventricular, 1. The locations of tumors producing back shift were: frontal, 3; frontotemporal, 1; fronto-

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It may be that there is a field for punch and aspiration biopsy. Certainly there is no harm in trying to make a diagnosis in advanced or inoperable malignancies by these methods. The physician may get enough idea of the nature of the growth to formulate a rational treatment. This may save the patient unnecessary radiation, for example.

It has not been my fortune to find either of the above methods otherwise to be especially useful. In my experience the material gained by these procedures is sparse. A few clumps of cells, with much granular debris and a scattering of red blood corpuscles, makes an interesting guessing contest with the odds slightly in favor of cancer over the field. The cell clumps often look more like musical notes than any kind of pathologic picture. There is no pattern by which infiltration of normal structures may be realized. The cellular detail is poorly defined. Occasionally a clump of cells may be identified as cartilage, fat, etc., but it would be a risk to the patient and to the surgeon to determine the treatment by this evidence alone in most cases. Of course, it is now considered good form to try some radiation treatment first. This being done, the diagnosis is effectively scrambled until recurrence or metastasis clarifies the nature of the original picture.

From this it may be inferred that I have a personal prejudice against the newer methods of biopsy. My own conviction in the light of experience is that the old fixed tissue stains give the greatest accuracy; that frozen tissue sections come next but are much inferior and that the surgeon had better place more reliance on his gross picture in doubtful cases; that punch biopsy stands still lower in the scale; and that aspiration biopsy is least reliable. It takes a good deal of guessing and imagination to state accurately what the material really is in the latter two types of biopsy. This may be due to inexperience on my part, but the most I have been able to do with these methods is to report "malignant," "cartilage," "fat," "no diagnosis," which are rather broad generalizations with little accurate information. If there is enough question about a diagnosis to warrant a biopsy, why not get a real specimen of the tissue for examination? If the patient has some inoperable, advanced malignant condition, on the other hand, suction biopsy may be all that is necessary to satisfy the curiosity of the attendant.

—John J. Morton, M.D.
Rochester, N. Y.

Training of the Clinical Pathologist

AT THE TURN of the century and up until 1920 there were very few clinical pathologists. With the evolution of medicine and with the development of various laboratory procedures, the field of the pathologist broadened so that, while tissue pathology was still the major field, the supervision and in many instances the actual work in other labora-

Editorials

Biopsy

EVERY NOW and then, and lately it seems with increasing frequency, a section of tissue is brought for microscopic examination. This is done on the assumption that a surgeon who is constantly removing diseased portions of the human anatomy also must know something about the differences between the normal and the pathologic appearances under the microscope. There is a measure of truth in this, provided that the surgeon has a natural curiosity about the reasons for his being a surgeon. And a goodly number of surgeons have acquired proficiency as pathologists, some even being rated as experts in special fields.

The main difficulties in microscopic diagnosis are centered about the granulomas and neoplasms, since the acute inflammatory lesions rarely cause trouble. From the time of Virchow, pathologists have been accustomed to prepare sections for examination so that a generous slice of the material can be shown. This fixed type of tissue block requires time for dehydrating and staining. The end result is a distorted desiccate of the original cells, but it gives a picture of the relationship to the surroundings, a very important requisite in the determination of malignancy. It is true that there have been pathologists in the past who have claimed to be able to diagnose malignancy from a single or a very few isolated cells. The majority of pathologists, however, do not assume this ability for themselves.

Attempts to study the cells with vital stains have been carried out. This would appear to be a logical method, but so far, except for the blood cells and some brain tumors, little has been done with it. It has not gained a hold as a popular method for the study of pathologic material.

In an endeavor to speed up reports on suspected material, several methods have come into being during recent years. In addition to frozen sections we have the punch biopsy in which a fragment is speared, hooked, and then severed by the outer sheath of a hollow needle; and the aspiration or suction biopsy in which a hollow needle is introduced into the suspected mass and suction made with a syringe so that some material is drawn up into the needle. This is then smeared on a glass slide, stained, and examined.

Experience with frozen sections is variable. Sometimes a diagnosis is easily made; for other sections, nothing definite can be said. The surgeon can make a diagnosis in practically every instance from the gross appearance alone if he is an accurate observer.

Specific Therapy in Acute Staphylococcal Sepsis

THE UBIQUITOUS staphylococcus is a biologic agent that causes a variety of infections, ranging from a relatively benign pyoderma to a fulminating and fatal septicemia. While most staphylococcal infections occur as localized lesions, occasionally the local defense mechanism breaks down, resulting in a blood stream invasion and the establishing of metastatic foci. The invasiveness of the staphylococcus is dependent upon certain characteristics of the bacterial cell, and at times upon potent exotoxins elaborated by the organisms. Consequently, staphylococcal bacteremia and septicemia should imply not only the presence of viable bacteria in the blood, but also their toxic soluble products. In general, the aim of therapy in acute staphylococcal sepsis is to keep the infection localized, and to prevent the dissemination of organisms and toxins through the tissues and blood.

It is generally recognized that a persistent bacteremia is attended by serious consequences for the patient. The mortality rate is high. Death is often due to an overwhelming toxemia. In recent years many investigators have attempted to elucidate the features of antibacterial and antitoxic immunity in patients with staphylococcal infections. Interest in the toxin-antitoxin relationship was heightened by the Bundaberg disaster of 1928 in which a number of children died shortly after being injected with diphtheria toxin-antitoxin. It was found that the bottle containing the prophylactic had been contaminated with staphylococci, and the recipients had been killed by a lethal staphylococcal exotoxin. Since then, through the work of Burnet, Dolman, Stookey, and Burky, the exotoxins of staphylococci have been more clearly defined. At the present time, many recommend the use of a potent staphylococcal antitoxin in the treatment of acute sepsis with bacteremia. It has been shown that the survival period is prolonged in animals injected intravenously with living staphylococci and treated with antitoxin as compared to untreated controls.^{1,2} Encouraging clinical results have been reported by those treating patients with antitoxin. It would appear that the antitoxin has a beneficial effect on the acute toxemia but that it does not prevent the establishment of metastatic lesions. It must be admitted that the antitoxins now available have a limited therapeutic value, and some patients are not apparently benefited by their use. This may be due in part to the fact that highly invasive strains of staphylococci may produce little or none of the soluble factors which the antitoxin neutralizes. Furthermore, the antitoxin has no demonstrable effect upon the living bacterial cell; in other words, it is not bactericidal in its action. One of the soluble factors elaborated by probably all pathogenic strains of staphylococci is leucocidin. This agent is destructive for leucocytes, and, since the role of phagocytosis is so important in the defense mechanism against staphylococci, it has been suggested by some investigators that the most valuable antitoxin would

tory branches had to be done by that individual. In all except the largest hospitals today the pathologist is expected to supervise hematology, serology, bacteriology, parasitology, biochemistry, and the rapidly expanding field of hormone and endocrine assay which requires the co-ordinated application of biochemistry, physiology, and pathology. Obviously the average hospital cannot afford specially trained experts in each of these fields, so that the practical solution is through the use of the clinical pathologist.

Conversely, the clinical pathologist cannot be an expert in all of the aforementioned subjects but does need more instruction than is offered in courses leading to the degree of Doctor of Medicine. A casual survey reveals very few medical schools or hospitals in the United States prepared to offer training in tissue pathology and simultaneously the additional training either to do or to supervise the work in the related subjects. In many hospitals associated with medical schools, special laboratory procedures are carried out by that division in the school. With only a few exceptions, clinical pathology is taught to medical students by the department of medicine and in many instances with complete disregard of the correlation which might be had in subjects fundamental to clinical pathology. As an example, it is not unknown or unusual to have one hypothesis and nomenclature of blood formation taught in histology, and a second in pathology, only to have both upset by the introduction of a third in clinical pathology.

As a prerequisite to special training in clinical pathology, a general rotating internship should be required. It should then be possible in three years of graduate work, devoting the major part of time to pathology, to have both formal courses and practical laboratory training in the other basic branches. Contact with patients should be encouraged, since frequently the proper interpretation of laboratory data depends on the correlation of clinical and laboratory findings.

It should be possible in at least the majority of class A medical schools for the department of pathology, in conjunction with other departments of basic sciences, to arrange courses of graduate instruction designed to give at least the knowledge for supervisory capacity. All medical schools should be able to offer the work in bacteriology and biochemistry, but there are many schools in which courses in hematology, serology, and parasitology are both inadequate and unsatisfactory. However, for at least five years, under the auspices of the American Society of Clinical Pathologists, refresher courses have been presented in tissue pathology and hematology which have served as a valuable medium of instruction and fulfilled a definite need in this regard. There is imperative need for graduate work and the time has come for medical schools to offer improved facilities in training clinical pathologists which will be on a par with those offered for other specialists in medicine.

—*Frank J. Heck, M.D.*
Rochester, Minn.

mine has remained in favor from year to year. Occasionally, an individual with a serious staphylococcal septicemia has recovered following treatment with neoarsphenamine. This sequence of events has also occurred in patients who have received no specific therapy. It would appear that the most promising results with neoarsphenamine are obtained in patients with infections involving the urinary tract. Unfortunately, little is known about the mechanism of the action of neoarsphenamine.

With the introduction of sulfanilamide and related compounds into the therapy of infectious diseases, it was the general hope that at last an effective specific agent or agents were available for the treatment of staphylococcal sepsis. The dramatic entrance of prontosil into the medical world was in the form of a report on its successful use in the treatment of a patient having staphylococcal septicemia. Such hopes were short lived. It is now generally agreed that, whereas prontosil and sulfanilamide are effective in the therapy of staphylococcal infections of the urinary tract, they possess little value in the treatment of deep-seated lesions and septicemia. Attention should be called to the important observations of Carpenter and Barbour,⁶ who, in well-controlled experiments, found that mice were protected against lethal doses of staphylococcal exotoxin when the toxin was mixed with sulfanilamide before injection.

Clinical and experimental data are accumulating, indicating that sulfapyridine is of considerable therapeutic value during the acute stage of staphylococcal septicemia. Long and Bliss⁷ have stated that sulfapyridine is the most effective chemotherapeutic agent that we possess against such infections. This statement is voiced by others. It has been shown that mice infected with lethal doses of staphylococci and then given sulfapyridine survive for much longer periods of time than normal controls or those given sulfanilamide.⁸ In vitro studies reveal that both sulfanilamide and sulfapyridine have a bacteriostatic and bactericidal action upon many strains of pathogenic staphylococci when added to whole defibrinated blood.⁹ The effects are more pronounced with sulfapyridine. In treating patients with sulfapyridine, it has been found necessary to maintain the level of the drug in the blood between 10 and 15 mg. per 100 c.c. for several days. The clinical results are less striking than those that are observed in the therapy of pneumococcal and streptococcal infections. Because patients may tolerate sulfapyridine poorly when it is given orally, it is often expedient to administer the sodium salt intravenously. In conjunction with sulfapyridine therapy, frequent transfusions may be necessary, and localized lesions should be drained at the proper time. Several patients at the University of Minnesota Hospitals with severe staphylococcal septicemia have been treated with sulfapyridine. The results have been most encouraging. It should be pointed out that the exhibition of the drug

be one containing a high titer of antileucocidin. Such an immune serum would be indirectly antibacterial, as well as antitoxic, since the organisms are presumably killed by being phagocyted. Antitoxins used in this country have little or no antileucocidin. Valentine and Butler² in England have recently reported on the therapeutic use of a serum containing antileucocidin, and the product merits further trial.

Many attempts have been made to introduce into patients therapeutic agents that will have a direct effect upon the organisms. While some of the procedures appear valid, experimental evidence concerning their bactericidal action is lacking. A method of serotherapy that is often used is the transfusion of a patient with the blood from an immune donor. This donor has either been actively immunized with organisms isolated from the patient, or has recently recovered from a staphylococcal infection. While patients recovering from a staphylococcal septicemia have a high titer of antitoxin in their blood as compared to normal individuals, it would appear more reasonable to use the more potent commercial antitoxins obtained from immunized animals. There is suggestive evidence, however, that convalescent human sera, in addition to antitoxin, have precipitins and agglutinins for the staphylococcus. But the results of this form of therapy in general have been discouraging, and more precise immunological and clinical data on the value of immune transfusions in staphylococcal sepsis are needed.

Julianelle⁴ has recently presented encouraging results in the treatment of patients with staphylococcal septicemia using an immune rabbit serum. He had previously found that all pathogenic strains of staphylococci possess an intracellular polysaccharide, which is different from the polysaccharide present in nonpathogenic strains. He had also observed that only the sera of patients recovering from severe staphylococcal infections contained precipitins for the specific carbohydrate of pathogenic staphylococci. On the basis of these observations, he administered to a group of patients with staphylococcal septicemia an immune rabbit serum containing a high titer of precipitins for the carbohydrate fraction of staphylococci. This type of therapy appears rational and merits further investigation on a larger group of patients.

Several enthusiastic clinical reports are available concerning the use of staphylococcal bacteriophage in the treatment of severe sepsis. It is difficult to correlate these clinical findings with the indifferent results obtained in animals experimentally infected and treated with bacteriophage. Available experimental evidence would indicate that bacteriophage therapy may actually be harmful.⁵ There is an urgent need for more carefully controlled observations in human beings to whom bacteriophage is exhibited before this form of therapy can be accepted for general use.

Various chemotherapeutic agents have enjoyed their era of popularity in the treatment of staphylococcal infections. Of these, neocarsphena-

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

SOME CURRENT PROBLEMS OF ANESTHESIA

HENRY K. BEECHER, M.D., BOSTON, MASS.

(From the Anesthesia Service, the Massachusetts General Hospital)

(Continued from the July issue)

MISCELLANEOUS

Preanesthetic Medication.—

Aims: Anesthesia is concerned not only with protecting the patient from pain during surgical operation, but also from fear of the operation. Alexander and Cullen (1936) discuss these points. Aims of preanesthetic medication are to bring about a minimum of fear, a maximum of confidence, depression of general metabolism, obtundation of reflex irritability (without jeopardizing the vital processes), and fortification against hazards of the operation or anesthesia to be undergone. In principle at least, these aims are as old as surgery itself. In ancient times mandragora and *Cannabis indica* were employed to dispel fear and later pain. In 1869, Claude Bernard demonstrated the value of preanesthetic medication (See Gwathmey's textbook) in laboratory animals.

Intravenous Morphine: While morphine sulfate has been used therapeutically for nearly 140 years, it is only comparatively recently that it has been used intravenously. About ten years ago the method began to be popularized in Europe. Betlach (1937) describes the sensations produced by intravenous morphine: "Some complain of dizziness, tinnitus, tachycardia, and a feeling of warmth. Fainting with a quick recovery occurs rarely. Vomiting follows intravenous injection less frequently than subcutaneous administration. . . ." At the Mayo Clinic from $\frac{1}{6}$ to $\frac{1}{4}$ grain is dissolved in 2 c.c. water and injected under sterile conditions; first about $\frac{1}{24}$ grain is slowly injected, and then thirty seconds are allowed to elapse. If no signs of idiosyncrasy have appeared, the drug is then injected very slowly until the desired effect is obtained. Chief uses for the intravenous administration of morphine are: as an adjunct to regional anesthesia, for analgesia in peroral endoscopy, as a supplement to a waning spinal anesthesia, for the rapid control of visceral colics and cardiac pain, for preoperative medication in emergencies. The advantages of intravenous administration over subcutaneous are that the drug can be administered at the moment needed, full analgesic effects are immediately obtained, and the dose can be regulated accurately.

Waters (1938) has presented a study of morphine, scopolamine, and atropine and their relation to preoperative medication and pain relief. This study of preanesthetic medication is to be reported in detail later.

may not prevent the formation of metastatic lesions. Sulfapyridine does not appear to have any effect upon chronic lesions, such as osteomyelitis. Whether staphylococcal antitoxin should be used along with sulfapyridine has not been established. A priori, it would seem that both should be given on the grounds that circulating exotoxin would be neutralized by the antitoxin.

Sulfapyridine offers a more hopeful outlook for patients with acute staphylococcal septicemia than we have had in the past. The rapid developments taking place in the field of chemotherapy will undoubtedly find new chemical derivatives which will be less toxic, and probably more effective against the staphylococcus. Promising drugs now under investigation are sulfathiazole and sulfamethylthiazole. Serotherapy will command more attention in the future. It is not unlikely that potent antibacterial and antitoxic sera will be available and will be administered simultaneously with some of the newer chemotherapeutic agents.

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—Wesley W. Spink, M.D.
Minneapolis, Minn.

last three is undoubtedly governed by the factors of alveolar ventilation, pulmonary blood flow, and the air-water distribution ratio (Widmark, Haggard). However, the final rate of elimination of the lipotropic substances, after a thirty-minute transition period, is determined primarily by the slow rate of diffusion of the substance from the fat deposits in the body (Ruigh [1939]). The final rate of elimination of an anesthetic agent which has a high oil-water partition coefficient is regulated chiefly by the duration of the anesthesia and the quantity of fat present in the body.

Barbiturates: In any consideration of the barbiturates, several points are of interest: Why do some of the compounds act more quickly than others, even though all have been administered intravenously, and why does prolonged action occur in some cases but not in others? In an attempt to explain why, upon intravenous injection of the sodium salts of barbital and phenobarbital, there is a marked delay in the onset of action, whereas with amytal, pentobarbital, and evipal anesthesia is produced promptly, Bush (1937) determined the apparent ionization constants of these agents. From these, the hydrolysis of the sodium salts and the acid-salt ratios at the pH of the blood were estimated; however, these values are such that there is no correlation apparent between them and the rate of onset of anesthesia.

Butler and Bush (1939) have considered the effects of N-methylbarbital and of N, N'-dimethylbarbital. The qualitative effects of these are similar. Apparent effects of small doses disappear quickly; but, following the administration of large doses, the first severe reactions are followed by prolonged, less intense effects. To account for this behavior they have suggested two plausible explanations: First, that the rate of inactivation, although initially high, may decrease as the duration of anesthesia increases; second, that in the animal body these substances may be transformed into less active compounds, these less active agents producing the aftereffects of large doses. The second hypothesis has been studied experimentally. Shonle, Keltch, Kempf, and Swanson (1933) have considered the question of elimination of barbituric acid derivatives in the urine.

They state that a molecule of amytal is five times as effective as a molecule of barbital and that a molecule of pentobarbital is ten times as effective in producing anesthesia in rats.

While 90 per cent of small doses of barbital are excreted, only from 40 to 50 per cent of large doses are excreted in the urine; so apparently the body can break down barbital.

Because of their large alkyl groups, barbituric acid derivatives such as amytal are less water-soluble and more lipid-soluble than barbital, and, therefore, they should be removed from the blood stream by the nervous tissue more rapidly than is barbital.

Amytal and pentobarbital are excreted in the urine of men and dogs only in traces, if at all, following administration of their sodium salts;

Premedication and the Quantity of Anesthetic Agent Needed: The use of premedication in anesthesia has several purposes, as pointed out above; among these is the aim of lessening the psychic shock to the patient about to undergo the ordeal of a surgical operation, by the production of a serene, acquiescent state of mind. When larger doses of such agents are employed, the aim is to diminish the quantity of anesthetic agent necessary to reach a given level of anesthesia. Calderone (1935) has measured the ether concentration in dog's blood at the onset of surgical anesthesia, again at the point of respiratory failure, without premedication, and then after morphine in doses comparable to those used clinically. The concentrations of ether in the blood, with and without morphine, were practically the same in each case for the production of surgical anesthesia or respiratory failure. The same result was found after subanesthetic doses of amytal were given as preliminary medication. This agent had no effect upon the blood-ether concentration necessary to produce surgical relaxation or respiratory failure. When doses of this barbiturate great enough to produce anesthesia in their own right were used, a little less ether was required for respiratory failure than when ether alone was used. In these barbiturate experiments there was little, if any, summation of effect in the clinical range. The additive actions were not striking. The real advantage of preliminary medication appeared to be, according to these experiments of Calderone, the mental relaxation and repose afforded.

Generalization on the above findings is impossible at this time, and, indeed, some doubt is thrown upon their accuracy by the more recent study of Robbins, Baxter, and Fitzhugh (1939). This group studied cyclopropane, not ether as Calderone did. Perhaps these two agents vary in regard to the effects of preanesthetic medication, but it seems unlikely. At any rate, Robbins and his associates found that in dogs, following the use of a dose of morphine considered to be comparable to that used clinically, the blood concentration of cyclopropane required to produce abdominal relaxation is reduced by 48 per cent, that required to abolish the wink reflex is reduced by 27 per cent, and yet the amount required for respiratory arrest is not reduced at all. The factor of safety with cyclopropane is thus increased. Similar results were obtained with amytal and sodium barbital premedication.

Elimination of Anesthetic Agents.—

Inhalation Agents: The lipid-blood partition coefficients (olive oil-water, as actually measured) are for the following substances: acetone, 0.23; ether, 3.20; cyclopropane, 34.20; divinyl ether, 41.30; chloroform, 100.00.

The last three are plainly of a different order of magnitude than the first two. These last three can be described as lipotropic. The overall rate of elimination of the first two and the initial period of elimination for the

thetia, review the literature on the subject. They describe a technique for the estimation of local anesthetics derived from para-amino-benzoic acid in cerebrospinal fluid, blood, and urine. Their conception of what constitutes the usual concentration of procaine used clinically is exactly twice the concentration considered to be the maximum allowable in this country. Their studies have been conducted in cats. They make the interesting observation that, if the spinal anesthesia be repeated an hour or two after the return of tendon jerks, the drug disappears more slowly and the anesthesia lasts longer. This is interesting in regard to the use of the "continuous" spinal anesthesia technique.

Only from 3 to 5 per cent of the injected dose of procaine (sub-arachnoid) was eliminated in the urine of both animals and man, even though very large doses were administered.

Their examinations of the blood indicate that only exceedingly small amounts are absorbed.

Koster, Shapiro, and Leikensohn (1938) have studied the concentration of procaine in the cerebrospinal fluid of the human being following subarachnoid injection in 122 patients who were placed in the Trendelenburg position.

Encephalography With Anesthetic Gases.—

Aird (1936) has worked out a procedure for testing gases for encephalography in experimental animals (dogs). Nitrous oxide and ethylene were found to be the most promising and better than air or oxygen, he states. He reports true anesthetic effects of some gaseous agents administered by the lumbar route.

Newman (1936) employed nitrous oxide for encephalographic injection in patients with rather poor radiologic results. No evidence of anesthesia or sedation was observed. Subsequent headache was greatly reduced. Better radiologic results were obtained with ethylene. The necessary period of hospitalization was reduced from three days when air was used to 1.85 days with ethylene (twenty-six patients). In one subject the spinal fluid pressure was followed for five hours after the injection. After one hour a negative pressure of 13 cm. of water was observed, presumably due to the rapid absorption of the gas. This required another hour to return to zero. The possibly serious consequences of this pressure change deserve consideration.

The use of anesthetic gases for encephalography appears to be questionable, not only on account of the uncertainty of pain reduction, but also because of their extremely rapid rate of absorption which subjects the central nervous system to a considerable negative pressure. This rapidity of absorption makes it necessary to reinject the gas if repeated pictures are required.

Anesthetic Agents and Resistance to Pneumococcal Infection.—

Much speculation and a considerable number of papers have been devoted to problems concerning the effect of alcoholic intoxication

but under the same conditions, barbital and phenobarbital are excreted as such. They suggest that amytal and pentobarbital are rapidly and completely destroyed in the body.

These workers have suggested that detoxification of the barbituric acids might be related to opening of the pyrimidine ring. Butler and Bush (1939) showed that such breakdown products were not in the two cases studied responsible for the prolonged effects of the barbiturates. They next attacked the problem of whether the loss of physiologic activity of N-methylbarbital and N-methylphenobarbital might be related to the accumulation of demethylated products. They showed that the activity of the methyl compound is always above that of the corresponding demethylated compound. This, as they point out, is compatible with the hypothesis that the N-methylbarbituric acids are demethylated, the reaction progressing rapidly at first, slowly later. Other hypotheses are not necessarily incompatible with the data presented; for example, a detoxifying mechanism which involved conversion to inactive compounds would be just as consistent with the data, if the rate of such a reaction proceeded rapidly enough.

To test the demethylation hypothesis, Butler and Bush gave intravenously to dogs injections of pure N-methylphenobarbital in anesthetic doses. None of this compound was recovered from the urine, but they obtained pure phenobarbital (4 per cent of the theoretical). Under similar circumstances, but using N-methylbarbital, the pure demethylated compound was recovered in the urine in amounts up to 44 per cent of the theoretical, while only from 2 to 3 per cent of the N-methylbarbital was recovered. Butler and Bush present data suggesting that their yields of demethylated products account for the disposition of about one-half of the N-methylbarbital and about one-quarter of the N-methylphenobarbital, thus indicating that demethylation must be in large part responsible for the shorter action of these methyl compounds. This does not exclude the possibility of other important reactions as well. Such appear to be especially likely in the case of N-methylphenobarbital. The data presented show only the average rate of demethylation, and the early high rate of detoxification may be due principally to some other process.

This work makes it quite clear that the course of anesthesia under the short-acting N-methylbarbituric acids may be influenced by the detoxification products. The piling-up of still active breakdown products is an undesirable factor here that must be reckoned with in any consideration of continuous or repeated injection procedures.

Weese (1938) states that the same depth of anesthesia was produced by the same dose of evipal in rabbits on repeated anesthetizations (eight) the same day. Chapman and Veal give indirect evidence against this.

The Fate of Drugs Used in Spinal Anesthesia: Bullock and MacDonald (1938), in considering the fate of drugs used in spinal anes-

The striking observation was then made that no macroscopic lesion developed in any of the intoxicated animals. The same significant results were found under ether or avertin anesthesia. Microscopically it was found in these rabbits that almost no leucocytic infiltration had occurred and that the bacteria were growing in the tissues in swarms, whereas in the nonintoxicated animals, great leucocytic infiltration occurred and no bacteria could be found in the sections after nine hours.

An outstanding observation is described in the following sentence: "Neither the intoxicated rabbits nor the anesthetized rabbit developed any lesion whatever at the site of infection until they began to recover from the narcosis, when there appeared a progressive edematous and hemorrhagic lesion which soon spread (from the flank) to the belly surface." This finding is of such importance in anesthesia that much more checking of the point in regard to the anesthetics is desirable than has yet been carried out. It would be of particular interest to know if the finding holds for the prolonged anesthesia common under avertin.

Subsequent studies showed that, if bacteria can grow uninhibited by the body's defenses for from three to five hours, inflammation developing after that may be unable to overcome them.

These findings appear to be of great clinical importance and, incidentally, support the attitude of many as to the questionable wisdom of using alcohol as a therapeutic measure when any infection is present.

Further experiments were carried out in vivo to show that alcoholic intoxication does not impair the phagocytic power of leucocytes. It was also demonstrated that alcohol intoxication or ether or avertin anesthesia produced no effect upon the number of nonmotile leucocytes in the blood of man or animals.

From these studies it seems clear that loss of immunity during alcoholic intoxication or ether or avertin anesthesia is due, not to a paralysis of leucocytes, but rather to their failure to emigrate. It is suggested that this failure to emigrate may be due to an effect of anesthesia or intoxication upon the vascular inflammatory mechanism; however, the evidence for this is by no means certain. It seems better to let the matter rest by saying that, although the mechanism is obscure, it has been shown that intoxication and anesthesia act to prevent the usual inflammatory reactions in the tissues.

Does Ether Anesthesia Protect From Anaphylactic Shock?—

Many attempts have been made to settle experimentally the question of whether ether anesthesia will protect from anaphylactic shock. Most of these studies were inadequately controlled, so that no positive conclusions could be made; yet one frequently hears it dogmatically stated that ether anesthesia will protect against shock from tetanus

and of anesthesia upon infection and immunity. In this literature two main facts (Pickrell [1938]) stand out: First, most observers agree that infected intoxicated animals die sooner than similarly infected but nonintoxicated ones; however, few of these studies have been properly controlled. Second, no satisfactory explanation for any resistance-lowering effect has been established.

Pickrell reviews the literature, starting with the findings of Koch in 1884, who observed that most of the people who became sick during cholera epidemics used alcohol to excess. Koch tested this in the laboratory and confirmed the observation in rabbits. The review is carried down to more recent times, through the outstanding paper of Capps and Colemann who showed that, for any particular age period, there was a definitely increased pneumonia mortality proportional to the degree of alcohol consumption. For the whole series (3,422 patients with pneumonia), "excessive drinkers showed a mortality of 49.87 per cent, moderate drinkers, 34.4 per cent, and abstainers or occasional drinkers, 22.45 per cent."

From the numerous papers reviewed the conclusion is inescapable that infected intoxicated animals die sooner than similarly infected nonintoxicated controls. Pickrell (1938) set out, first, to determine whether alcoholic intoxication lowers the resistance to pneumococcal infection, and, second, to discover how this is effected, if so. During the course of these studies he also included a few observations upon the effects of ether and of avertin anesthesia in regard to resistance to infection. The primary concern of this paper was not with the ordinary anesthetics. It is regrettable that, if ether and avertin were to be referred to at all in this excellent paper, more details were not given, as, for example, in regard to depth of anesthesia and its duration in all cases.

Rabbits were used in these studies. In all experiments the procedure was to immunize a group of animals by the injection of Type I anti-pneumococcus serum, to intoxicate some, and to infect all; in addition, intoxicated and nonintoxicated nonimmune controls were infected intradermally with the same dose of Type I pneumococci.

It is clear from the experiments carried out that loss of immunity to Type I pneumococcus occurs during alcoholic intoxication and during ether or avertin anesthesia. (As already suggested, more data are desirable in the case of the anesthetics.)

Following intracutaneous injection of Type I pneumococcus, the non-intoxicated immunized group showed macroscopically only a minute erythematous lesion. These animals did not develop a positive blood culture. They survived.

The nonintoxicated nonimmunized rabbits "developed a large, edematous, hyperemic and purpuric lesion." These animals all developed a positive blood culture and died within eighteen hours.

peripheral action on the bronchial musculature than to any central nervous system action. In Dale's theory of anaphylaxis it is assumed that anaphylactic contraction of plain muscle is caused by histamine or histamine-like substances. Farmer (1938) has shown that anesthetics belonging to various chemical groups inhibit the histamine contraction of plain musculature (intestinal strips from guinea pigs). This inhibiting action of the anesthetics can be enhanced by substitution of aliphatic radicals with increasing carbon atoms, substitution of a phenyl group, and halogenation. Apparently the inhibiting action is increased by procedures which increase anesthetic potency. It seems probable from the data presented that the inhibitory action described is due to the relaxing effect of anesthetics upon plain muscle.

Anesthesia, the Fetus, and the Newborn Infant.—

The recent introduction of numerous new sedative and anesthetic agents into obstetrics has had much to do with focussing attention upon the response of the fetus and the newborn infant to the anoxic effects of some of these drugs. An interest in this problem is certainly not new in many medical centers; but it is chiefly in the past few years that a general awareness seems to have developed that, with the use of certain agents in obstetrics, or perhaps with the unwise use of these agents, the infant may pay too high a price for the mother's comfort, as Dr. Irving has put it. Corrective measures have too often arisen only after tragic experience. One good result of these experiences has been to stimulate an interest in the physiology of the fetus and the newborn infant. Profit from such studies extends beyond obstetrics into all medicine, for the intelligent interest of obstetricians in asphyxia neonatorum has done much to bring about a general knowledge of the evils of anoxia in patients of all ages.

It has been repeatedly demonstrated that respiratory movements are not initiated at birth. The beginnings of respiratory activity were recently shown by Barcroft and Barron (1936) to originate early in embryonic life.

They have shown in the sheep (which has a gestation period of about 157 days) that rhythmic trunk movements associated with ordinary respiration are developed between the thirty-eighth and forty-ninth days of fetal life. At this stage they cannot be elicited by asphyxial conditions of the blood. At about the forty-ninth day the frequency of these movements becomes more rapid, and they become more powerful. After the fiftieth day the rhythmic movements disappear as a spontaneous phenomenon, but stoppage of the blood flow in the umbilical cord will elicit them. The article by Barcroft (1938) contains further information.

The failure to recognize that the fetus has a special physiology was responsible for much misconception here. Snyder and Rosenfeld (1937, a) have amply demonstrated this. They have succeeded when

antitoxin, for example. Quill's report (1937) of the death of a patient is enough to throw serious doubt on this statement. He describes the case of a man who died under ether anesthesia, apparently of anaphylactic shock following the administration of tetanus antitoxin, at the end of an operation for a gunshot wound of the abdomen. (Unfortunately this case is confused by the fact that the man had received a blood transfusion.)

In discussing the paper on Koontz and Shackelford referred to below, Harris recalled Dew's work on hydatid disease. Dew states: "Owing to the abolition of the anaphylactic state by general anesthesia, grave symptoms rarely, if ever, occur at operation, even if much hydatid fluid is spilt into the wound. There is no doubt that operations on these cases under local anesthesia carry with them some risk of anaphylaxis, and I have personally observed one patient operated upon by a colleague in whom a fatal result with all the symptoms of anaphylactic shock occurred." Dew also says that, if fluid is spilled at the time of operation, delayed anaphylactic phenomena sometimes appear after the effects of the general anesthesia have worn off. Tropical surgeons are said to be so completely convinced of the protective action of ether anesthesia that it is axiomatic that all operations for suspected hydatid disease (including exploratory puncture) should not be done under local anesthesia.

Koontz and Shackelford have made detailed observations of the response of guinea pigs sensitive to foreign protein, when injection of shocking doses of the protein, both with and without ether anesthesia, have been made. Sixty-five sensitive animals were injected under ether anesthesia; fifteen died. Sixty-nine sensitive animals were injected without anesthesia; thirty-three died. Of importance also is the observation that all of the unanesthetized group that survived showed marked symptoms of anaphylaxis, while none of the anesthetized group did. Of course, the anesthetic may have masked some of the clinical signs of anaphylaxis. The conclusion appears to be justified, however, that ether anesthesia significantly reduces the percentage of deaths from anaphylaxis when animals sensitive to foreign protein are given shock-provoking injections during the period of anesthesia. The considerable number of deaths that did occur even under anesthesia make it clear that, if the results obtained in the guinea pig are transferable to man, it is not a safe procedure to give tetanus antitoxin to patients under ether anesthesia without previous tests for sensitivity. On the other hand, it does appear probable, although certainly not proved, that a patient who was sensitive to horse serum would be less likely to have a reaction if the injection were made while he was under ether anesthesia.

Farmer (1938) recalls Besredka's demonstration that anesthesia may prevent fatal anaphylactic shock in guinea pigs. It has been suggested that this protecting action of anesthetic agents is more likely due to

is not initiated in the child at birth but extends far back into embryonic life. Failure to accept observations made long ago is probably due to the fact that fetal apnea may easily be caused by the depressant drugs and anesthetic agents used at birth, this apnea incorrectly being considered normal.

It seems plain that respiratory failure of the newborn infant must be regarded as suppression of previous normal activity rather than failure of some new mechanism to begin functioning at birth. The question is not what causes the first breath, but rather, when apnea occurs, what factors have caused suppression of the normal activity.

In recent years great increases in the use of preliminary medication at childbirth have made it apparent that much needs to be learned about this practice. Clinics like that maintained at the Boston Lying-In Hospital are doing much to bridge the gap between the pharmacologist and the clinician through controlled studies. In that clinic Clifford and Irving (1937) have studied problems of analgesia and anesthesia in relation to the newborn infant. "The ultimate fate of present methods of analgesia may well hinge on the price the infant must pay for the mother's comfort."

Several pertinent facts are reviewed (*loc. cit.*) concerning the normal physiology of the fetus and the newborn infant. As already described, the human fetus makes rhythmic respiratory movements in utero which continue as breathing, following birth. In utero the full-term human fetus exists normally in a state of cyanosis, with a mean capillary oxygen unsaturation (11.1 volumes per cent). At birth the circulation of the placenta is impaired by the retracting uterus, with increased unsaturation of the capillary blood, so that at birth the arterial blood of the fetus contains less oxygen than the maternal venous blood. Cyanosis at birth is, then, not abnormal; it becomes so only if prolonged.

Intrauterine anoxia of the fetus is accompanied by an accumulation of lactic acid in the fetal blood. The respiration fails, and the blood pressure falls in the presence of severe anoxia. The skin is blanched and cold at birth. When such fetuses are delivered at term, the onset of respirations is much delayed or never appears. Trauma to the fetus through cerebral edema or hemorrhage may produce this same clinical picture at birth.

It has been shown that respiratory movements of animals in utero can be retarded and arrested by morphine, the barbiturates, ether, and other drugs. When this is the case, great difficulties are presented in the way of establishing extra-uterine breathing, and these may account for pathologic prolongation of the cyanotic state of these newborn infants. Such fetuses may be pallid and atonic.

In this study of Clifford and Irving, 410 cases were considered. Using the above criteria, 63 per cent of the infants in the pentobarbital-sodium amytal group (260 cases) were physiologically normal, whereas in the morphine-pantopon series (100 cases), only 43 per cent were physio-

others failed or obtained half truths, by a new approach to observation of the fetal respiratory system, new in that they dispensed with the complicating factor of anesthetics, except when specifically studying their effects. They employed a technique which involved inhibition of labor. They have studied the fetuses of rabbits, cats, guinea pigs, and human beings.

Outstanding findings are that the fetal respiratory movements are depressed or abolished by oxygen want.* However, this alone does not establish that some oxygen want may not have been responsible for the initiation of the movements. It is conceivable that this is true and that further oxygen want might depress them. Barcroft (1938) has discussed this possibility. Snyder and Rosenfeld consider that the depression effected by oxygen want is evidence that the carotid body mechanism is not functioning in the (rabbit) fetus before birth. Carbon dioxide deficit results in depression or apnea of the fetus. This shows that a certain level of carbon dioxide is essential to maintain fetal respiration; yet excess carbon dioxide has little or no effect. It is evident from these data that the fetus is peculiar in comparison with the mother; the failure of oxygen want or carbon dioxide excess to stimulate respiration is unlike the adult (unless, of course, the stage had then been reached where these factors depress respiration).

The rate of respiration of the fetus varies according to its stage of development. It is several times more rapid in postmature fetuses than in premature ones.

The respiratory system of the fetus is peculiarly sensitive to anesthesia; respiratory movements of the fetus may be abolished at a level of analgesia at which respiration is not impaired in the mother. Ether, nitrous oxide, divinyl ether, paraldehyde, phenobarbital, pentobarbital, and chloral hydrate all were found to have depressing actions. Cyclopropane was found to be the least depressant. Great significance must be attached to the finding of the extreme sensitivity of the fetus to the depressant effects of the common anesthetic agents.

Observations of the fetal movements transmitted through the abdominal wall were made in a series of women near term. (Snyder and Rosenfeld, 1937, b.) It was thus possible to recognize unmistakably spontaneous fetal movements which continued at a regular rhythm for many minutes. Two chief types were recognized: one is characterized by a rapid rate (about 60 per minute) and a shallow excursion; the other, the less common type, appears as a sudden deep excursion, at a slower rate (about 15 per minute). The first resembles thoracic respiration, and the latter, abdominal breathing.

Dye studies, microscopic lung examinations, and various experimental studies indicate that the breathing of amniotic fluid is a normal function of fetal respiration. From the studies available, the conclusion is inescapable that in man, as well as in animals, the respiration

*However, see Barcroft above.

C. Removal of mucus and debris under direct vision with a laryngoscope is indicated in severe asphyxia with the placement of an intra-tracheal tube in such cases.

D. The use of CO_2 is probably contraindicated, at least not indicated.

Eastman (1936, b) has carried out fetal blood studies in an attempt to evaluate the role of anesthesia in the production of asphyxia neonatorum. The bloods of fifteen infants delivered without anesthesia were used as controls. He finds that chloroform (four cases) has no demonstrable effect on fetal blood oxygen saturation, but is undesirable because of its toxic effects upon the mother. Ether (eight cases) produces a slight depression in the fetal blood oxygen saturation, but insufficient to injure the fetus. When nitrous oxide-oxygen (twenty-eight cases, various proportions) is administered to mothers, as 85:15 or weaker, for periods of less than five minutes, some fetal anoxia may be produced, but without harm to the baby. When the nitrous oxide mixture contains only 10 per cent oxygen or less, marked degrees of fetal anoxia occur with occasional profound asphyxia neonatorum.

A study of the effect of obstetric anesthesia upon the oxygenation of the maternal and fetal blood has been made by Smith (1939). Determinations were made of the oxygen content of arterial and venous blood of women during labor. Three groups of mothers and their infants were similarly studied at the moment of birth during routine deliveries under ether, under nitrous oxide-oxygen, and under cyclopropane anesthesia. It was observed that ether anesthesia elevated the maternal oxygen capacity and the oxygenation of maternal venous blood. Fetal oxygenation appeared to be satisfactory. It is interesting to observe in passing that all of the patients except one received ether by open cone; notwithstanding this, the blood of the fetus was better oxygenated with ether and room air than was the case when 80 per cent oxygen was used with cyclopropane.

Under cyclopropane, the maternal blood showed considerable elevation of oxygenation in both the arterial and venous samples. Curiously, the blood of infants delivered under cyclopropane was poorer in oxygen than that of those born under ether, poorer even than that of those (reported elsewhere) delivered without maternal anesthesia.

In this study no definite relationship could be observed between anoxemia in the fetus and apnea of the newborn infant. Fetal anoxia is probably only one of several factors which operate to produce apnea.

Cyclopropane was found to be present in the fetal blood in almost as high concentration as in the maternal blood; but only about one-half as much nitrous oxide was found in the fetal as in the maternal blood.

Smith concludes that, judging "by biochemical data, cyclopropane as an obstetrical anesthetic would appear to be perhaps less safe for the infant than the clinical appearance of the mother would indicate."

logically normal. Active measures of resuscitation were required in 3 per cent of those receiving barbiturates, while 23 per cent of those receiving morphine-pantopon required active resuscitative measures. Abnormally prolonged cyanosis was present in 23 per cent of the former group, while it was present in 38 per cent of those given an opiate. The only two infant deaths of the study occurred in the pantopon series. These and other facts are presented which indicate that the use of morphine or pantopon in obstetric analgesia is unsatisfactory for the mother and dangerous for the infant.

Clifford (1934), in a consideration of the obstetric management of premature labor (304 premature infants), found that, in every case (seven cases) in which morphine was administered to the mother within one and one-half hours of delivery, the infant died. At birth these infants showed embarrassed respiration, and they presented the clinical picture of asphyxia, respiratory center failure. Clifford, in a further investigation (*loc. cit.*), found that, in 850 consecutive premature infant deliveries, 752 mothers received no morphine within four hours of delivery, with an infant mortality of 36 per cent. Ninety-eight mothers received morphine within four hours of delivery, with an infant mortality of 60 per cent.

Common obstetric parlance describes any baby that fails to breathe at birth as "asphyxiated" whether this be due to oxygen lack, cerebral hemorrhage, or congenital defect. Eastman (1936, a) prefers that the term "asphyxia neonatorum" be applied to infants who fail to breathe at birth, because of an inadequate supply of oxygen during labor.

Irving has shown that when mothers received no analgesic drugs or anesthesia, 98.1 per cent of the babies breathed immediately after birth. When the mothers received nitrous oxide-oxygen and ether, 80 per cent of the babies breathed immediately after birth; when the mothers received barbiturate analgesia with scopolamine, rectal ether, or paraldehyde, from 50 to 65 per cent of the babies breathed immediately after birth.

The work of Snyder and Rosenfeld and others makes it clear that the treatment of apnea at birth should consist of an effort to preserve and safeguard a mechanism already in active existence.

Matters of interest to the anesthetist in the treatment of asphyxia neonatorum are (Eastman):

A. Posture.

1. To accomplish the drainage of mucus from the respiratory passages. (Lowering of 15° from the horizontal is enough.)
2. Avoidance of any posture which might aggravate a beginning cerebral hemorrhage.

B. A pressure of 14 cm. H_2O is necessary to expand the alveoli in the newborn infant's lung.

Levi and Krinsky (1936) report that the intravenous or intramuscular administration of coramine decreases the duration of postpartum anesthesia due to nembutal and paraldehyde used together.

Whatever the merits or demerits of spinal anesthesia in obstetrics, Mallinson (1938) has not presented very convincing arguments against the use of spinal anesthesia in pregnant patients. He describes a death under spinal anesthesia of such a patient who had one day previously experienced a "heavy loss of blood" by vagina, this following ten days of "continuous slight bleeding." She was described as pale. Although no data are provided as to the character of the blood, presumably she had suffered great blood loss from a ruptured ectopic pregnancy. Whether the patient is pregnant or not, spinal anesthesia is hardly the method of choice in a potential shock patient who has experienced great blood loss.

Graffagnino (1938) describes the use of peridural anesthesia in gynecology and obstetrics, as have also Graffagnino and Seyler (1938).

Anesthesia in Warfare.—

Schmid (1937) presents a German viewpoint in regard to the alleviation of pain in military medicine. His paper takes up the problems of transportation and anesthesia in caring for the wounded during war. The author divides the early care into three phases: (1) Making [the wounded] fit to be transported and their transportation; (2) field surgery [in the field hospital]; (3) later transportation and further treatment.

He considers certain fundamental points in the organization of the sanitary service, the importance of testing the value of methods in peacetime, and the lessons learned in the last war. He divides anesthesia into two phases:

I. Treatment of the pain of wounds, under which he considers:

1. Morphine and pantopon
2. Scopolamine-eucodal-ephetonin
3. Keeping [the wounded] quiet

II. Anesthesia for operation, under which he considers the merits, uses, and limitations of:

1. Local anesthesia (which can be extensively used)
2. Chloroform (still first in his opinion among agents for field surgery)
3. Ethyl chloride
4. Ether and vinethene
5. Gas anesthetics (nitrous oxide, ethylene, acetylene)
6. Rectal anesthetics (rectal ether-oil + avertin)
7. Intravenous anesthetics (pernocton, eunareon, and evipan)

He concludes that the range of anesthetics for field surgery is much the same as in 1914—chloroform, ether, novocain, and morphine, with

And he states further that "the use of ether appears to offer the least disturbance of normal oxygenation of fetal blood."

Schreiber (1938) has observed in a study of 500 patients with symptoms of cerebral damage that most cases of cerebral birth injury are associated with apnea at birth, and further that the depressing effect upon the respiratory center of birth analgesics given in greater than pharmacologic dose is directly related to the degree of apnea. The extent of the apnea is related directly to the severity of the cerebral symptoms after birth, and this, in turn, is directly related to the amount of damage to the brain tissue. It seems evident here that the use of analgesics in greater than pharmacologic dose may be, in many instances, the causative factor of fetal anoxia, with resultant brain damage in the infant.

Further information is presented in the panel discussion on cyanosis of the newborn by McKhann, Clifford, Green, Baty, Farber, and Teel (1938). An editorial in the *Journal of the American Medical Association* (1938) presents summarizing statements concerning asphyxia of the newborn infant.

Draper and Whitehead (1938) have attempted to determine in dogs the margin of safety between the states of analgesia and respiratory arrest produced by ether, divinyl ether, and chloroform. Their findings are in accord with those of others and are of interest because of the care with which they have been obtained. Ether, the least potent of the three agents, had the greatest margin of safety. Chloroform was most potent, but also had the lowest margin of safety. Divinyl ether occupied an intermediate position on both counts. Resuscitations from forty-five deliberate, standardized overdoses of divinyl ether and from forty-two ether overdoses were in all cases successful. After forty-nine overdoses of chloroform, there were six dogs, or 12 per cent, that could not be resuscitated.

Danforth and Danforth (1938) have studied the influence of pentobarbital sodium upon the duration of labor. They state that the first stage of labor is more than two hours shorter in primiparous women who have received pentobarbital than in those who have not; this is not so in multiparas. They suggest that the barbiturate hastens the dilatation of the cervix. Not enough details as to dosage, controls, etc., are given to allow analysis of the data.

Graham and Pettit (1938) have added a barbiturate (allyl-isopropyl barbituric acid) to an ether-oil solution for rectal administration at delivery. From 101 cases, they consider that prolongation of labor two hours in primiparas and five hours in multiparas (as compared to standard textbook estimation) the greatest objection to the use of the procedure.

Bourne and Pauly (1939) have discussed the use of pentothal and thioethamyl in obstetrics.

count. A minimal list of factors to be considered in this regard has been discussed by Beecher (1939).

Important from the point of view of physical and chemical qualities are potency or narcotic strength, solubility in air and blood, and explosibility. From the more strictly biologic aspect of the question, the elements of importance are controllability of the route of administration, side-effects and toxicity of action, adequacy of physiologic effects for the task at hand, specificity of action, and elimination. Statistical requirements are considered in relation to the mass of data necessary to permit dogmatic statements to be made as to death rate and general safety. It was pointed out that anesthesia literature, perhaps more than that of any other division of medicine, is shot through with claims wholly unsupported by available evidence. No one can object if a person wishes to report a few hundred anesthetics with no deaths. In certain cases, such reports are desirable, as, for example, when a new anesthetic agent is being tried and no one man has had opportunity to acquire a really adequate personal series. Strenuous objections can be raised and should be, if such reports contain any attempt to draw conclusions as to the safety or death rate of the new agent or to make comparison with other agents with a possibly similar or lower death rate.

Whether we like it or not, the fact remains that, if anesthetic agent A has a death rate of 1:1,000 cases, we need data of the order of 10,000 cases with about ten deaths before we can make any statements as to the death rate of that agent. (It might be argued that six deaths are adequate; however, for a conservative estimate ten are safer.)

If the death rate of anesthetic agent B is 1:10,000 cases, we need the order of 100,000 cases with, again, about ten instances of death attributable to the agent, in order to make any statement as to the death rate of that agent.

It is sometimes said that the death rate directly attributable to ether anesthesia is 1:10,000. In order to prove that another agent is better than ether in this respect, we must have, then, not less than about 100,000 cases of the other agent, under comparable conditions, if we are to prove that the other agent excels or even equals ether as far as death rate is concerned.

Stating the foregoing in general terms, we must deal with so many cases that the square root of the number of deaths is not greater than about one-third of the number of deaths.

Analeptics.—

Study of the analeptics is progressing at such a rapid rate that there is a temptation to confuse promising experimental findings with clinical observations. To avoid such a mishap, several of the recent clinical applications of these agents will first be referred to, with a later consideration of experimental findings of interest, and finally some reference to attempts to explain the action of this group of agents.

the addition of seopolamine-eucodal-ephetonin (to take the place of veronal), ethyl chloride, and intravenous anesthetics.

An English point of view is presented by Mitchiner and Cowell (1939) who consider the problem of anesthesia for patients injured in warfare (air raids). Wherever possible, nitrous oxide-oxygen should be used, they state, and, if necessary, it should be fortified with ether. "In no circumstances should spinal anesthesia be used in such cases, for the resultant fall in blood pressure is very hard to combat. . . ." They consider local anesthesia undesirable in regions already edematous and conducive to the growth of organisms. Nerve block may be useful, but it is often impossible to determine ahead of time the limits of operation. The patient's mental condition is such that it is usually better that he be unconscious. "Chloroform (except in hot climates) . . . must not be used . . . for the risk of cardiac failure is very great."

Chambon, Hubert, and Périer (1937) state that, in dogs poisoned by phosgene, nitrous oxide or cyclopropane is better for anesthesia than ether. The animals are less "sensitive" to the two former agents.

The "Ideal" Anesthetic Agent.—

The qualities expected in an "ideal" anesthetic gas have been considered by SeEVERS and WATERS (1938) from the points of view of the four individuals chiefly concerned. The *patient* wants an induction of anesthesia which is rapid and pleasant and a recovery period free of discomfort. The *surgeon* asks that the agent be nonexplosive, that it not increase bleeding, and, most important, that it effect complete muscular relaxation. The *anesthetist* looks for a good margin of safety, and asks that the agent be unchanged on elimination, with little functional or organic injury during or after exposure, that it be potent enough to allow a high percentage of oxygen to be administered during anesthesia, and finally that interchange of the anesthetic between atmosphere and tissues be so rapid as to allow swift controllability. The *manufacturer* expects the "ideal" anesthetic gas to be one which can be simply and cheaply made, easily purified, and stable during long storage. No known agent fulfills all of these requirements, although nitrous oxide most nearly approaches the ideal. Its lack of potency is so serious a handicap that one must search for other agents.

In a carefully documented review, SeEVERS and WATERS (1938) describe the chemical and biologic qualities of the gaseous anesthetic agents and point out their clinical potentialities and limitations.

Proprietary anesthetic agents are appearing on the market at an increasingly rapid rate. The advocacy of first one and then another of these changes so rapidly in some institutions, that a yardstick of unchanging criteria must be at hand if new agents are to be evaluated accurately and safely. If the good are to be recognized and employed and the bad discarded, a number of factors must be taken into ac-

by the barbiturate could be elevated by the subcutaneous use of benzedrine sulfate. Reifenstein and Davidoff (1938) concur in reporting this effect following intravenous use of the drug. In one of their cases great hypertension was produced very rapidly, and in at least two of ten patients, hypertension of undesirable degree occurred.

Michelsen and Verlot (1939) have used benzedrine in an effort to control avertin anesthesia. They report that avertin anesthesia can be shortened in rabbits and in patients by the use of this agent.

The use of benzedrine in combatting the hypotension of spinal anesthesia has been described by Tovell (1936).

Coramine in Barbiturate Depression in Man: Schube (1936) administered doses of four barbiturates respectively to a fairly large series of men. In each case the subject was so deeply "asleep" that moderate shaking and pinpricking failed to arouse him. Coramine was administered in 5 c.c. doses at ten-minute intervals until consciousness was restored. Unfortunately only one control was used for each barbiturate. Since individual reaction to the barbiturates is notoriously variable, this is not enough; however, it was observed that those in the series receiving coramine recovered consciousness in a matter of minutes, while the controls did not awake for some hours. No serious untoward reactions to the coramine were encountered here. A good bibliography is included.

Metrazol and Avertin: Schlaepfer (1936) reports that metrazol shortens the duration of avertin anesthesia in man by about one-fourth.

Experimental Studies: Picrotoxin, metrazol, and coramine have all received much attention recently in both the clinic and the laboratory. On examining the rather numerous contributions concerning these agents, Werner and Tatum (1939) found much to be desired and, therefore, undertook further individual and comparative studies of the three drugs.

They found that single doses of coramine do not cause complete arousal of rabbits depressed with from 20 to 30 mg. per kilogram of nembutal intravenously, and neither do single doses save or prolong the lives of animals receiving 110 mg. per kilogram intraperitoneally. On the other hand, single doses of metrazol and picrotoxin do cause complete arousal of rabbits depressed with sublethal doses of intravenous nembutal, and they save the lives of rabbits depressed by 110 mg. per kilogram of intraperitoneal nembutal. When this dose of nembutal is exceeded, only picrotoxin is effective in single dose. The conclusion can be drawn that picrotoxin is the more effective analeptic for dealing with the severe grades of nembutal depression.

When used in doses short of convulsant ones, metrazol and picrotoxin were not found to be significantly depressant, yet coramine appeared to be depressant in doses which were not convulsant. When convulsions occurred under metrazol and picrotoxin, the ensuing depression appeared due to the exhausting effects of the convulsions rather than primarily to the drugs.

Clinical Use of Picrotoxin: The value of picrotoxin in combatting poisoning by barbiturates appears to be fairly well established clinically. Kohn, Platt, and Saltman (1938) have treated four patients poisoned by barbiturates with picrotoxin. Of these, three recovered and one died. (They offer a brief review of the literature on this subject.) One patient recovered after receiving a total of 671 mg. picrotoxin over four days.

Rovenstine (1938) reports the use of picrotoxin in four patients suffering from barbiturate poisoning, with three recoveries. In Case 1 picrotoxin was given in 3 mg. doses at irregular intervals, 129 mg. being given over nine hours in a 5 per cent glucose and normal saline infusion. In Case 2 picrotoxin 48 mg. were given intravenously in one hour. In Case 3 picrotoxin, 122 mg. was given over many hours. In Case 4 picrotoxin 2,134 mg. were given over seven days; the patient died. A good bibliography is appended.

Maloney (1936) recommends the preliminary use of 2.0 c.c. 0.3 per cent picrotoxin intramuscularly immediately preceding the use of evipal anesthesia. This procedure eliminates respiratory accidents, he states on the basis of forty patients who received evipal anesthesia for an average duration of 58.9 minutes.

Whenever a patient is brought into the Emergency Ward in deep coma with small, fixed pupils, corneal anesthesia, low blood pressure, shallow respiration, râles in the lungs, and a fast, weak pulse, barbiturate poisoning should be suspected. Bleekwenn and Masten (1938) have reported six such cases treated with picrotoxin. The treatment recommended consists in the following:

1. Wash out the stomach even though the drug was ingested many hours previously. (Barbiturates delay gastric emptying; peristalsis is diminished or halted by these agents. Large quantities may remain in the stomach for a long period of time.)
2. Administer oxygen continuously.
3. Administer picrotoxin intravenously until pupillary and corneal reflexes have returned. Give 1:1,000 solution at the rate of 1 c.c. per minute. The depth of respiration improves first, and a rise in blood pressure occurs. The quality of the pulse improves and the rate becomes slower. The return of corneal or pupillary reflexes or twitchings indicates that the convulsive stage is near. Administration of picrotoxin can be resumed when the patient begins to lose the gains made. Bleekwenn, as have others, used from 24 to several hundred milligrams of picrotoxin over a period of hours.
4. Administer parenteral fluids with dextrose (and sucrose for diuresis).

Nosworthy (1937) and Raginsky (1938) give further information.

Clinical Use of Benzedrine: Myerson, Loman, and Dameshek (1936) reported that benzedrine shortened the duration of amytal narcosis. They (Myerson and co-workers) reported that hypotension produced

Strychnine they found to be ineffective under the above conditions; coramine was only a little better, while metrazol was often effective in large doses, but less effective than picrotoxin.

Nonconvulsive doses of picrotoxin usually stimulate respiration of anesthetized animals, but in normal dogs or in decerebrate dogs and cats no stimulation of the respiration occurs from the injection of picrotoxin until convulsive doses are given. This failure of the agent to stimulate the respiration of unanesthetized animals except in convulsive doses, plus the fact that a decrease in depth of anesthesia is frequently observed following the injection in anesthetized animals, as well as the prolonged effect of the stimulation here, serve to set this drug apart from the ordinary respiratory stimulants.

Marshall and his associates (1937) group the respiratory stimulants as follows:

1. Agents which act reflexly through general afferent stimulation (subcutaneous injections of ether, camphor in oil, distilled water, for example).
2. Those which act reflexly through the sinoaortic nerves (cyanide, coramine).
3. Those which act by improving the blood supply and oxygenation of a depressed respiratory center (epinephrine, ephedrine, oxygen).
4. Those which appear to act on the respiratory center directly (carbon dioxide, caffeine, metrazol).
5. Those which act by decreasing the depth of narcosis and restoring the subject more nearly to normal (picrotoxin).

The ability of analeptics to bring about general awakening or to arouse single central nervous functions is slight in the deeper stages of anesthesia. The question then arises whether analeptic phenomena (if a true antagonism is exhibited) are dependent upon the limit of the ability of the single anesthetized elements in the central nervous system to be influenced antagonistically, or, on the other hand, whether they are due to too small a number of points of attack for the analeptic. Koll (1937) has subjected these questions to experimental study.

His experiments were made on the flexion reflex of the whole hind leg or of a Semitendinosus-Vastocrureus-Preparation (S.V.P.) of the cat, in part with simultaneous observation of the crossed extension reflex. The lower portion of the spinal cord was isolated by cutting it across in the lower thoracic region, or the animal was decerebrated.

In lighter stages of anesthesia, cardiazol is capable of exercising considerable awakening effects upon the spinal reflex mechanisms with normal strength of stimulation, which, however, diminish quickly with increasing depth of anesthesia. In very deep anesthesia, only a very slight awakening of the reflex takes place with maximal strength of stimulation. The slightly awakened reflex cannot be augmented further by continued administration of cardiazol. With further giving

The actions of coramine and metrazol were found to be characterized by early peak effects, whereas the maximal action of picrotoxin was delayed as much as from fifteen to thirty minutes. Allowance must be made for this in therapy.

When rapid, complete arousals from great barbiturate depression are produced by metrazol or picrotoxin, such arousals may be accompanied by dangerous convulsions; therefore, Werner and Tatnm point out that immediate, complete reversal of the depression should not be attempted in the treatment of severe barbiturate poisoning, but, rather, that one should be satisfied with a lesser degree of steady improvement.

It was found that picrotoxin and metrazol, administered in comparable quantities, are inactivated at about the same rate; coramine, however, appears to be inactivated much more slowly.

Whitehead and Draper (1939) recall that Maloney and Tatnm found coramine more or less effective in stimulating the respiratory center when depressed by urethane, chloral hydrate, ether, or avertin, but ineffective against barbiturate depression, as have others. Lendle found that coramine stimulated the respiration when depressed by morphine.

Whitehead and Draper (1939) in an experimental study on dogs found no evidence that coramine increased the ease or speed of resuscitation from ether respiratory depression. When respiratory depression was produced by chloroform, coramine appeared to increase the mortality.

Marshall, Walzl, and LeMessurier (1937) have attempted to determine under what conditions of respiratory failure respiration can be reinstated and continued by the use of picrotoxin and the nature of its stimulating action on the respiration. Compared with it are strychnine, coramine, and metrazol. Observations were made on dogs and cats.

It has been shown (Marshall and Rosenfeld [1936]) that denervation of the carotid sinuses and aortic receptors under deep phenobarbital anesthesia is followed by respiratory failure. Under certain other anesthetics this does not occur. Marshall and his co-workers have also recently shown (*loc. cit.*) that, in animals greatly depressed by phenobarbital and morphine, the administration of oxygen appears to be equivalent to denervation of the sinoaortic receptors in the production of respiratory failure.

The conclusions reached by Marshall, Walzl, and LeMessurier (1937) are that picrotoxin is very effective in reinstating respiration when failure is due to phenobarbital anesthesia plus carotid sinus inactivation, and from overdosage with chlorbutanol, paraldehyde, or avertin fluid. Picrotoxin is less effective in overcoming urethane overdosage. It is useless against ethyl alcohol overdosage.

Picrotoxin and metrazol were found to be the most effective anti-anesthetics, then followed by benzedrine, caffeine, and ephedrine in descending order. Strychnine as used here shows no antianesthetic power.

Cutting and Koppanyi (1938) have used massive intravenous infusions of isotonic glucose or saline solutions, in volumes weighing from one-fourth to three-fourths the body weight in cats and dogs which were anesthetized by sodium barbital or sodium phenobarbital. The duration of anesthesia has been shortened to from one-third to one-half that of controls, with the doubling of the early elimination of these drugs in the urine. When massive infusions were utilized, animals receiving two or three minimum lethal doses of sodium barbital have recovered completely. The significant observation has been repeatedly made that, unless infusions were started and pushed with vigor within about one-half hour after the administration of fatal doses of the barbiturates, the infusions were without avail. Apparently the infusions are effective only if they can prevent critically high levels of the agents from accumulating in the nervous system.

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of cardiazol, it remains at an approximately constant height. Thus, a limitation of the effect of cardiazol is evident. The reflex aroused by this means is characterized by a very steady course, which does not differ considerably from the normal, except by some protraction.

The awakening experiments with strychnine led to entirely analogous results. Here also, with very deep anesthesia and very strong stimuli, a limitation of effect is apparent which cannot be exceeded by further giving of the alkaloid. The reflex aroused by strychnine shows, on the other hand, a quick, transitory "beginning convulsion" and, in its further course, a clonic character.

At the limit of effect of cardiazol, the result of arousing can still be extraordinarily increased by strychnine, and in the opposite case, cardiazol is still capable of producing a great increase in the reflex at the limit of effect of strychnine.

Miller and Spiegel (1939) have used the well-known antagonism between picrotoxin and barbiturates in a study of the sleep-waking mechanism. Their study is directed toward a localization of effects of these agents. They find that picrotoxin is able to "awaken" rats from barbiturate sleep after removal of the cerebral cortex (except for a small medial strip of the pyriform lobe).

Tartler presented experimental evidence for attributing both stimulant and depressant qualities to certain convulsant drugs when given to white rats under sodium barbital narcosis. Maloney (1936) has analyzed the stimulant-depressant action of caffeine, coramine, and metrazol in rats and rabbits under sodium barbital narcosis. He found it was fairly simple to find the optimal dose in the case of metrazol in the anesthetized rat and caffeine (alkaloid) in the anesthetized rabbit, since with these there is a broad plateau of efficiency. In other experimental groups, however, the suddenness of the change from maximal stimulation to unmistakable depression on the one hand or fatiguing convulsions on the other, makes it practically impossible to fix upon a surely optimal dose. With such a narrow margin of effective therapeutics, considerable hazard accompanies the use of these agents, at least in animals.

In studying the antianesthetic effects of some convulsants in the albino mouse, Hjort, deBeer, and Fassett (1938) found that the concurrent presence of anesthesia (*n*-propyl-*o*-tolyl urea and sodium ethyl [1-methyl-butyl] barbiturate) decreases the toxicities of picrotoxin and strychnine by more than 100 per cent and lowers the toxicity of metrazol to about one-half. The M.L.D. of caffeine is not affected by anesthesia. Anesthesia slightly increases the toxicity of ephedrine and increases the toxicity of benzedrine fivefold.

In judging cerebral analeptics on the basis of their effectiveness as antianesthetics, picrotoxin appears to be the safest and benzedrine the least safe. Benzedrine should be used during anesthesia only with great caution.

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Review of Recent Meetings

REVIEW OF THE AMERICAN SURGICAL ASSOCIATION

J. DEWEY BISGARD, M.D., OMAHA, NEB.

Presidential Address: The Lag Phase of Wound Healing. Allen O. Whipple, New York City.—The lag period in wound healing, or that interval until severed tissues are united sufficiently to have tensile strength, under favorable conditions lasts four days but may be prolonged by a number of local and general factors. The duration is determined by such local factors as tissue trauma, blood supply, hemorrhage, exudate, bacteria (number and character), and foreign bodies; and by such general factors as age of the individual, hydration and dehydration, nutrition (supply of available protein and vitamins, particularly vitamin C), and blood (anemia).

To shorten the lag period treatment should be directed toward preventing and correcting (1) hypoproteinemia by ingestion of high protein diet preoperatively and administration of whole blood, blood plasma, or amino acids, if the oral route is impossible; (2) vitamin deficiency (vitamin C essential to collagen formation and vitamin K to prevent bleeding in cases with a prothrombin deficiency); (3) circulatory inadequacy and anemia; (4) infection; (5) trauma to tissues (trauma to be avoided by delicate handling and sharp knife dissection). By attention to these details, the incidence of leakage along suture lines and disruption of wounds can be materially reduced.

Symposium on Fluid and Electrolyte Needs of the Surgical Patient:

The Structure of the Blood in Relation to Surgical Problems. John P. Peters, New Haven, Conn. (by invitation).—In salt-depleted patients the administration of salt-free fluids not only fails to correct the salt deficiency but increases depletion by washing salt from the body. The distribution of fluids in the body is determined by relative osmotic pressures (and this by the distribution of salts) not only in the cells, interstitial spaces, and blood stream but also in the body cavities, such as the gastrointestinal tract. Hypotonic fluids taken by mouth or sufficient salt should be given in capsules to make the fluids isotonic within the gastrointestinal tract. Also, hypotonic solutions are severe irritants to the jejunum. Normally, water taken by mouth becomes isotonic in the stomach before reaching the jejunum. For this reason solutions introduced directly into the jejunum should be isotonic. Furthermore isotonic solutions rest the bowel. To rest the gastrointestinal tract as completely as possible, absolutely nothing should be given by mouth. This excludes the sucking of ice chips for it must be remembered that "ice becomes water when it melts."

The Preservation of Blood. David C. Bull, New York City (by invitation), and Charles R. Drew, Washington, D. C. (by invitation).—"The intelligent use of preserved blood required knowledge as to wherein and to what extent it differs from fresh blood." Studies show that the white cell and platelet counts fall 50 per cent or more in the first two or three days but that the erythrocyte count

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remains little changed for a month though the individual cell shrinks and much of its hemoglobin is to be found in the plasma. Potassium passes from the cells into the serum and sodium passes from the serum into the cells. This phenomenon is hastened by trauma but is little influenced by the type of preservative or container. Though the plasma potassium rises as much as tenfold and potassium is definitely a toxic substance, the transfusion of preserved blood should be safe on this score except when large amounts of blood are given rapidly in conditions in which there already exists a hyperpotassemia. Diffusion between serum and cells can be minimized by a narrow-neck bottle which diminishes the area of surface contact.

Prothrombin in stored blood falls rapidly to 50 per cent of its original value where it remains for some time.

Thus, for purposes of supplying plasma proteins and replacing erythrocytes stored blood is entirely adequate. In the treatment of infections where available leucocytes are desired in the transfused blood and in the treatment of hemorrhagic diatheses where platelets and prothrombin are desired fresh whole blood is definitely superior to stored blood.

In discussion, Waltman Walters, Rochester, Minn., pointed out that, in addition to laboratory and other data, one should utilize the clinical evidence of dehydration, such as the urinary output, evidence of toxemia, and the dry tongue, in determining fluid and electrolyte needs of patients. Large quantities of chlorides may be lost from the body in the bile draining from biliary fistulas and this source of loss should be taken into account. On several occasions Walters has utilized a jejunostomy for temporary feeding of patients in a poor state of nutrition (presumably deficient in vitamin C and proteins) before carrying out such surgical procedures as gastric resection.

Owen Wangenstein, Minneapolis, Minn., in discussion, remarked that water and hypotonic solutions applied directly to the jejunal mucosa cause a violent inflammatory reaction of this membrane with edema and in certain instances ulceration, as stated by Peters.

Distention in a large part results from swallowed air and this distention contributes to death in the presence of peritonitis and obstruction. By excluding air-swallowing by means of dividing and exteriorizing the cut ends of the esophagus, dogs with intestinal obstruction can be kept alive for long periods of time by maintaining fluid and electrolyte balances. In a few patients nitrogen balance has been maintained by administration of large quantities of bovine plasma. Reactions have followed such administration.

In aged patients in whom the cardiovascular system is impaired, fluids should be administered subcutaneously rather than intravenously.

The Plasma Proteins of Preserved Blood, John Scudder, New York City (by invitation).—Proteins are needed by surgical patients not only to prevent the edema of hypoproteinemia but also to promote normal wound healing and to fortify the liver. To provide these needs in a readily available supply blood plasma has proved very satisfactory. Plasma and its proteins are very stable and can be stored for as long as three years without deteriorating. Likewise plasma from donors belonging to Groups A and B can be given to any recipient without fear of a transfusion reaction. Plasma can be salvaged from the whole blood stored in blood banks when the blood is discarded at its expiration date.

Sodium Chloride Metabolism of Surgical Patients, Walter G. Maddock, Ann Arbor, Mich. (by invitation).—Diseases of or operations upon the alimentary tract often interfere with the normal intake of sodium chloride and at the same time

may cause abnormal losses of this important electrolyte." With the knowledge of the normal standard salt requirements and with some guidance from determinations of the blood chlorides, the proper salt balance can be maintained. As a working basis the normal salt requirement of an individual varies from 5 to 10 Gm. daily. In restoring salt in depleted patients it may be calculated that 0.5 Gm. of salt per kilogram of body weight is necessary for each 100 mg. per cent that the plasma chlorides are to be increased to normal. Sodium chloride is lost mainly in sweat and urine, very little being lost in the stool. There is definite danger of administering too much sodium chloride by the routine use of salt solution without regard for the quantity of sodium chloride so given. If fluids in addition to the salt requirements are administered, these should be salt-free. The administration of too much sodium chloride results in salt retention in the tissues and this in turn to the retention of water and as a result edema. Edema may thus result from salt retention as well as hypoproteinemia. Blood chlorides cannot always be relied upon as a guide to sodium chloride needs. Under certain circumstances, salt may pass directly into the tissues as rapidly as given and be retained by the tissues in spite of a low blood chloride level.

Loss of Fluids and Salt Associated With Suction Drainage of the Gastrointestinal Tract, Grover C. Penberthy, and (by invitation) J. Logan Irvin, Detroit, and R. Mayo Tenery, Philadelphia.—In the presence of such drainage of the gastrointestinal tract nutrition and water and electrolyte balances have to be maintained by parenteral route unless the suction drainage is periodically discontinued or the Miller-Abbott type of tube passed into the terminal portion of the ileum. It is possible in the presence of an intestinal obstruction with suction applied low in the ileum to maintain large quantities of the bowel and at the same time to assimilate large quantities of water and food by absorption from the bowel above the level where suction is being applied. The unabsorbed residue is removed by suction. Under these circumstances it is necessary to maintain adequate intake (output studies as a guide to supplementing parenteral fluids to maintain water and electrolyte balance). Often with suction applied low in the ileum an adequate intake can be maintained by mouth. Nutrition can be maintained more adequately by this route and patients are infinitely more happy when they are able to take food and water by mouth.

Plasma Loss in Acute Intestinal Obstruction, Jacob Fine, Boston (by invitation).—"Continuous distention of the small intestine in the dog produces a fatal loss of plasma volume. Studies on the mechanism involved show (1) that this is a phenomenon specific to the small intestine and does not occur when the colon, gall bladder, and other hollow organs are distended; (2) that it is not due to dehydration; (3) that it is not due to distention of the peritoneal cavity. Decompression of the intestine stops the loss of plasma and facilitates its return to the circulating blood. Desoxycorticosterone also inhibits the loss of plasma due to distention of the small intestine." The loss of plasma and death resulting from this loss are in some way related to distention. Clinical studies have corroborated these experimental observations.

Plasma Loss in Shock as Affected by Therapy, A. S. Minot, St. Louis (by invitation).—"Vasoconstriction associated with shock causes an increase in capillary permeability with transfer of plasma from the blood stream into the tissues. Under these circumstances too rapid or too liberal administration of fluid and electrolytes may lead to complications which at times are as serious as those which arise from failure to supply them in sufficient quantity. "In patients in poor state of nutrition or in whom there is either localized or general injury to capillaries, it is particularly difficult to maintain the proper distribution of admin-

istered fluids. Massive edema may occur while the blood stream remains dehydrated or even becomes progressively more dehydrated. Under these conditions the administration of colloid is an indispensable factor in the restoration of fluid and electrolyte equilibrium." Under these circumstances salt solution washes out protein and after the loss of plasma absorption from the skin and bowel is impaired.

Hypoproteinemia and Its Relation to Surgical Problems, I. S. Ravdin, Philadelphia.—"The serum proteins are the major factors in keeping fluids in blood vessels. Too much attention has been paid to the administration of water and salt and not enough to the forces that keep these in blood vessels." Hypoproteinemia causes gastrointestinal edema and thereby retards gastrointestinal motility. This edema by involving the gastroenterostomy stoma may obstruct this outlet and cause the syndrome of vicious cycle. In addition the edema of hypoproteinemia delays and impairs wound healing contributing to leakage along suture lines and to wound disruption. Protein protects the liver against injury and aids materially in its repair and regeneration. In this respect it shares a place with carbohydrates so that diets designed for this purpose should contain high protein as well as high carbohydrate values. "The parenteral administration of amino acids has not corrected hypoproteinemia in our cases."

Fluid and Nutrition Maintenance by the Use of an Intestinal Tube, W. Osler Abbott, Philadelphia (by invitation).—In cases of chronic gastrointestinal disease requiring operative relief, management is often difficult because of the starvation which has preceded operation and the period of limited nutritional intake which necessarily follows operation. While the maintenance of a fluid and electrolyte balance can be remedied and maintained for a period by the parenteral administration of solutions, there is good evidence that in the presence of a pyloric obstruction jejunal feeding is preferable. Nutrition, particularly the assimilation of protein, can be provided much more satisfactorily by this route. For this purpose the author has devised a double lumen tube which is passed through the gastroenterostomy stoma at the time of operation. The proximal lumen which opens into the stomach is used to aspirate this viscus, while the distal lumen opens at a short distance down the distal loop of the jejunum and through it a liquid diet and fluids can be administered. One of the diets used for this purpose consists of peptinized skimmed milk containing 6 Gm. of dextrose to each 100 c.c. All solutions injected through the tube are isotonic. In cases of intestinal obstruction a long tube which empties intestinal contents down to the lesion allows the oral administration of fluids, electrolyte, and food, much of which is assimilated.

Parenteral Protein Replacement With Amino Acids, Robert Elman, St. Louis.—"Various types of patients suffering from protein deficiency and unable to ingest sufficient protein nourishment by mouth have been treated by the intravenous injection of fluid containing electrolyte, glucose, and amino acids. The amino acids were obtained by the enzymatic hydrolysis of casein. Nitrogen balance has been achieved with regularity, indicating utilization of the injected nitrogen. Evidence of serum albumin regeneration has also been noted in a few cases as has improvement in the general clinical picture." With the improved preparations of amino acids recently used there have been no reactions, no phlebitis and no precipitation, the complications previously observed.

The Proper Preparation of Solutions for Intravenous Therapy to Allergic and Fever Reaction, Carl W. Walter, Boston (by invitation).—Fluids for parenteral administration can be prepared economically in hospitals which utilize such solutions in large volumes. The preparation of such solutions demands meticulous

care to insure chemical purity. Not only must the solutions be chemically pure, but they must be delivered into the blood stream in this state.

In discussion of the above papers Dallas B. Phemister, Chicago, Ill., pointed out that the need for red blood cells must be remembered in considering replacement therapy. The administration of whole blood during operation under certain circumstances permits a more prolonged meticulous execution of the operation. Shock may accompany the loss of plasma under a variety of conditions, as illustrated in a case of thrombophlebitis. In this case there was a rapid loss of plasma into the tissues of the leg.

Damon B. Pfeiffer, Philadelphia, Pa., presented an ingenious method for calculating and recording the fluid and electrolyte balance of patients. By recording the figures calculated from blood chemistry studies on a graphic chart similar to a temperature chart the status and fluctuations of the electrolytes can be observed at a glance.

The Question of Drainage Following Cholecystectomy, Irvin Abell and (by invitation) Irvin Abell, Jr., Louisville, Ky.—To evaluate the necessity for drainage following cholecystectomy results in 500 cases were analyzed. In this group there was a mortality of 2 per cent. In 391 cases it was possible to carry out the ideal cholecystectomy and the abdomen in these cases was closed without drainage. Drainage was instituted in 109 cases. There were 74 cases of acute cholecystitis; 34 of these were drained. From these results there was no evidence to justify routine drainage following cholecystectomy and no evidence to indicate the necessity of drainage following ideal cholecystectomy. It is possible that drainage is conducive to leakage from the stump of the cystic duct.

John A. Wolfer, Chicago, Ill., in discussion stated that in animals the stump of the cystic duct becomes necrotic and separates distal to the constricting ligature with little or no repair of the duct at the site of separation for a considerable period of time. Leakage, however, is prevented by the accumulation of a fibrinous exudate which firmly seals the amputated stump.

Charles G. Mixter, Boston, Mass., added that, if stones are left in the common duct, leakage may occur from the stump of the cystic duct. For this reason it is desirable in certain cases to make a cholangiogram before closing the abdomen.

Physiological Factors Regulating the Level of the Plasma Prothrombin, Jonathan E. Rhoads, Philadelphia (by invitation of Walter E. Lee, Philadelphia).—The effectiveness of vitamin K therapy in combating prothrombin deficiency has certain limitations and is dependent upon liver function to a large extent. In dogs with biliary fistulas the vitamin K value falls slowly; whereas, in animals in which the liver has been severely damaged by chloroform poisoning or has been surgically removed the vitamin K and prothrombin values fall very rapidly. Such liver damage produces prothrombin deficiency by direct action and not merely through interference with bile salt formation. This type of prothrombin deficiency responds poorly or not at all to vitamin K.

Autopsies in three patients who failed to respond to vitamin K therapy revealed severely damaged livers. In such patients treatment should be directed primarily to restore liver function because only with restored function will vitamin K therapy become effective. To restore function the administration of large quantities of carbohydrates and proteins either by mouth or parenterally is indicated.

William D. Andrus, New York City, in discussion noted that it has been shown that, regardless of the dosage, vitamin K cannot be raised above 100 per cent.

istered fluids. Massive edema may occur while the blood stream remains dehydrated or even becomes progressively more dehydrated. Under these conditions the administration of colloid is an indispensable factor in the restoration of fluid and electrolyte equilibrium." Under these circumstances salt solution washes out protein and after the loss of plasma absorption from the skin and bowel is impaired.

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has healed and there has been no reactivation of the disease following closure of the ileostomy; others have become promptly reactivated.

In discussion **Harvey B. Stone**, Baltimore, listed three types of results which may be expected from ileostomy in ulcerative colitis: (1) patients who fail to improve after ileostomy; these should have a resection of the diseased portion of the colon or a total colectomy if satisfactory surgical risks; (2) patients in whom the disease fails to heal but they retain good health with the ileostomy present; (3) patients in whom the colon becomes healed and the ileostomy can be closed. As an aid to determine whether the colon has healed and closure of the ileostomy is feasible, the colon is filled with 2 liters of salt solution and an examination made of centrifuged sediment from this solution after it has been expelled for the presence of red blood and pus cells. If these cells are not present or are few in number, it may be assumed that healing has taken place. Ileostomy should be performed before the disease becomes advanced as judged by failure to improve promptly under adequate medical management and by the x-ray evidence of a loss of haustrations of the colon.

Frederick W. Bancroft, New York City, reported one case which has remained entirely well eight years after closure of an ileostomy.

Vernon C. David, Chicago, called to mind that with healing of ulcerative colitis polyposus may develop and subsequently one or more of these may undergo malignant degeneration. This sequence has been observed in three cases by David.

Edwin M. Miller, Chicago, suggested that before closing an ileostomy the colon be given a functional tolerance test by collecting material discharged from the proximal loop and injecting it into the distal loop.

The Diagnosis and Surgical Management of Leiomyomas and Leiomyosarcomas of the Stomach, **Frank H. Lahey**, Boston.—These tumors are very uncommon but not rare. They constitute 36 per cent of all benign gastric neoplasms. They ulcerate and commonly cause severe hematemesis and also obstruction, and are prone to become malignant. Adequate x-ray examination readily reveals these lesions. Seven cases were reported. The tumor in four showed malignant degeneration. Because of this danger a wide resection by either subtotal or total gastrectomy should be done. The prognosis is very good.

In discussion **Frederick A. Collier**, Ann Arbor, Mich., stated that some of these tumors which appear by the ordinary staining methods to be leiomyomas may prove to be neurogenic in origin when studied by special staining methods. An experience with two such cases was reported.

Abdominal Neoplasms of Neurogenic Origin, **Henry K. Ransom**, Ann Arbor, Mich.—Sixteen abdominal tumors of neurogenic origin were reported. Seven arose from or involved the stomach, four the small bowel and five were independent, mainly retroperitoneal. Five gave no symptoms and were found incidentally. The retroperitoneal tumors may arise from the sympathetic ganglia. "These tumors may simulate a variety of lesions such as carcinoma of the stomach, colon or rectum as well as pancreatic cysts and retroperitoneal sarcoma." They may produce serious complications, such as intestinal obstruction, internal fistulas involving the bowel or bladder and occasionally they become malignant. Complete excision results in cure and, since they grow slowly, incomplete excision where complete removal is impossible is indicated because it gives a long period of relative cure.

In discussion **John J. Morton**, Rochester, N. Y., reported that the location of these tumors and their relation to vital structures may make excision hazardous and

Studies Relative to the Pathogenesis of Cholecystitis and Acute Pancreatitis. J. Dewey Bisgard and (by invitation) Charles P. Baker, Omaha, Neb.—In the goat the pancreatic duct empties into the common bile duct (below the cystic duct) permitting the pancreatic juice and bile to mix, and pancreatic enzymes to pass into the gall bladder and bile into the pancreatic duct in the presence of an obstruction of this common passageway. A similar common passageway exists in 50 per cent or more of human beings. By producing temporary obstruction of the common duct in the goats above the pancreatic duct, stasis of bile in the gall bladder alone resulted; whereas, temporary constriction below the pancreatic duct produced in addition to stasis of bile, reflux of pancreatic secretions into the gall bladder and in some animals passage of bile into the pancreas. The presence of bile in the pancreas in all but one instance produced acute hemorrhagic pancreatitis. Pancreatic secretions in the gall bladder in the presence of stasis produced in each instance complete or partial necrosis of the wall of the gall bladder with regional peritonitis with and without perforation of the wall of the gall bladder. Five animals surviving the acute insult developed chronic cholecystitis, three of them with bile pigment stones. In all five, the gall bladder wall had become secondarily infected. Temporary biliary stasis alone produced no permanent pathologic change in the gall bladder wall, but in two animals infection became superimposed and resulted in subacute cholecystitis. In other words, stasis merely rendered the gall bladder vulnerable to infection in the latter group and vulnerable to the digestive action of pancreatic enzymes in the former group.

John A. Wolfer, Chicago, Ill., in discussing this paper, recalled his report in 1931 of similar results produced in the wall of the gall bladder of the dog by introducing pancreatic juice into the gall bladder by direct injection and by conducting the juice from the cannulized pancreatic duct into the common bile duct. India ink instilled into the common duct could be recovered later from the gall bladder. Cases with acute gangrenous cholecystitis present pathologic pictures similar to those presented by these animals in which there was reflux of pancreatic secretions.

Evarts A. Graham, St. Louis, stated that it is very doubtful that the pathogenesis of cholecystitis is as simple as presented in these experimental animals. It does not answer the fact that cholecystitis develops in adult life when the anomalous duct system exists from birth; furthermore it does not explain the high incidence of gall bladder disease of "John Bull" and the low incidence of "Uncle Sam."

Ileostomy. Henry W. Cave and (by invitation) Wm. F. Nickel, Jr., New York City.—In the treatment of intractable ulcerative colitis ileostomy has proved to be not only a palliative but often a curative operative procedure. It also has a definite place in the preoperative preparation of patients subjected to partial or complete colectomy and as an emergency procedure in the treatment of patients with impending perforation, obstruction, and gross hemorrhage. Ileostomy should be preceded, when it is an elective operation, by the rehabilitating measures of transfusions, restoration of vitamin, protein, and water balance and the administration of carbohydrates. Ileostomies have been complicated by prolapse of the bowel through the stoma, retraction of the stoma, hemorrhage, and intestinal obstruction. These complications can be minimized by complete division of the ileum, by the anchoring of the mesentery to the peritoneum and by exteriorizing both open ends of the loop. Subsequent resection of the large bowel is facilitated by implanting the open ends of the loop in separate incisions.

Always a difficult question to decide is when it is safe and proper to re-establish continuity of the intestinal tract. There are a number of cases in which the colon

I. A. Bigger, Richmond, Va., discussed a personal case of traumatic aneurysm of the abdominal aorta in a boy. At a first-stage operation the abdominal aorta was partially occluded above the aneurysm and several weeks later an aneurysmorrhaphy was accomplished with cure.

Rudolph Matas, New Orleans, discussed his case in which the abdominal aorta was successfully ligated and partially occluded. He also stated that Bigger's case was the first recorded successful repair and cure of an aneurysm of the abdominal aorta.

Cardiovascular Symptoms Presented by Patients Having Cavernous Hemangiomas and Varicose Veins, Walter E. Lee and (by invitation) Norman E. Freeman, Philadelphia.—Four patients presenting cavernous hemangiomas and varicose veins were discussed. In three of these individuals there was reflux of sufficient quantity of blood into the angiomas to produce disturbed cardiovascular physiology. A relative measure of the blood refluxed into the angiomas and varices can be had by a simple method. The leg is drained of blood and a tourniquet applied. It is then immersed in a jar of water and the tourniquet released. After the leg fills with blood, the water displaced is measured.

Although these lesions do not pulsate, they communicate with the arterial side, probably through arterioles.

Osteohypertrophy was a prominent feature in two patients. In one a defect in the lymphatic valves was also present, resulting in a chylangioma of the scrotum and thigh. "Ligation of communicating veins with defective valves brought about relief of symptoms in three of the patients." These communicating veins can be identified by diodrast angiography.

Arteriovenous Fistula: Experimental Observations and a Critical Review of Eighteen Clinical Cases, Emile Holman, San Francisco.—Arteriovenous fistulas were produced between the aorta and vena cava in puppies. There immediately developed a shrinkage in the size of the heart from hemorrhage into the venous side, followed by dilatation of that portion of the vascular system included in the short circuit; namely, heart, proximal arteries, and proximal veins. With dilatation there developed an increase in blood volume, and the signs produced by arteriovenous aneurysms of peripheral vessels, including ultimately the signs of cardiac failure.

Blood volume is not increased, Mont R. Reid, Cincinnati, pointed out in discussion, by the presence of an arteriovenous fistula until heart failure ensues. Cardiac failure regardless of cause is accompanied by an increase of blood volume, and the failure and not the fistula is the causative factor.

Relative Local Efficiency of Sulfanilamide, Sulfapyridine, and Sulfathiazol in Contaminated Wounds, J. Albert Key, St. Louis, and (by invitation) Charles J. Frankel, Baltimore.—In a series of rabbits and dogs compound fractures of ribs were made and these fractures inoculated with a virulent culture of *Staphylococcus aureus*. In addition the wounds in three groups were filled with crystals of sulfanilamide, sulfapyridine, or sulfathiazol. A fourth group was used for controls. Many of the controls failed to develop infections. Sulfanilamide was more effective than the other products in preventing infection. When placed into joints and serous cavities these chemicals produced little or no reaction. In wounds they were productive of an increase in exudate but did not otherwise alter wound healing.

The effectiveness of the direct application of sulfanilamide in preventing infection in wounds in man as originally reported by Jensen, Johnsrud, and Nelson has been well established.

difficult. An experience with a large retroperitoneal tumor in which two operative attacks were necessary to accomplish removal was reported.

Heparin in the Prevention of Peritoneal Adhesions, Edwin P. Lehman and (by invitation) Floyd Boys, University, Va.—In a previous report (*Ann. Surg.*, March, 1940) evidence was presented that heparin introduced into the peritoneal cavity of dogs was followed by the re-formation of 25 per cent of divided adhesions as compared with the re-formation of approximately 150 per cent of divided adhesions in control groups. Three out of twenty-four dogs died of intraperitoneal hemorrhage.

In a subsequent group of animals in which hemostasis was more meticulously executed, there were no hemorrhages. Also, there was no evidence of interference with wound healing.

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From similar studies in cats, **Harvey B. Stone, Baltimore**, pointed out in discussion, it has been found that quantities of heparin less than 1,000 units are relatively ineffective. The best results follow 1,000 units as the immediate initial dose supplemented by 1,000 units each on the two successive days.

The Prevention of Ischemic Gangrene Following Surgical Operations Upon the Major Peripheral Arteries by Chemical Section of the Cervicodorsal and Lumbar Sympathetics, Idys Mims Gage (by invitation) and Alton Ochsner, New Orleans. Sudden occlusion of major peripheral arteries results in ischemic gangrene necessitating amputation of an extremity unless an adequate collateral circulation is rapidly established. Associated with sudden occlusion there is set up reflex vasoconstriction which contributes to the ischemia and interferes with the establishment of collateral circulation. By chemical section of the regional sympathetics vasoconstriction can be immediately released. This is accomplished by infiltrating these regional sympathetic ganglia (cervicodorsal or lumbar) with novocain for a temporary effect or with alcohol for a prolonged or permanent effect. Chemical section was also advocated as a preoperative or postoperative measure to all operations upon the major peripheral arteries.

Discussing this paper, **Rudolph Matas, New Orleans**, noted that collateral circulation can be evaluated and can be promoted by the use of the Matas compressor. Transfusions may be useful.

Experimental Studies on the Occlusion of Large Arteries, Herman E. Pearse, Rochester, N. Y.—Many ingenious devices have been utilized in attempting to devise a method by which large arteries can be gradually occluded and thereby permit the establishment of a collateral circulation. The first successful method, as here reported, was accomplished by placing a strip of cellophane around the abdominal aorta in dogs. The foreign body reaction in the perivascular tissues causes a large ring of scar tissue to form around the aorta. As this scar gradually contracted it completely occluded this vessel.

Emile Holman, San Francisco, recalled that **Van Allen** has utilized this same principle to cause fibrotic contracture of the lung.

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Emile Holman, San Francisco, recalled that Van Allen has utilized this same principle to cause fibrotic contracture of the lung.

Aneurysm of the Abdominal Aorta: Successful Treatment by Ligation, Daniel C. Elkin, Atlanta, Ga.—A patient with a large aneurysm of the abdominal aorta at its bifurcation was relieved of pain and other symptoms by partially occluding the aorta just above the aneurysm with two ligatures of cotton tape. This technique is essentially the same used by Matas in his case. Circulation in the legs was not disturbed.

blood can be obtained by applying the photoelectric cell to a fold of skin. Records made by this device showed almost instantaneous changes in the oxygen saturation of the hemoglobin with changes in the oxygen content of the inspired gas. Inhalation of carbon dioxide caused a rapid fall which began immediately. The curve was immediately reversed following inhalation of pure oxygen. The anoxic curves resulting from nitrous oxide anesthesia and from sedation were presented.

Roy D. McClure, Detroit, pointed out that the damage produced in the brain and other tissues by anoxia may appear late. Often the damage produces slight and only transitory symptoms and only occasionally grave, progressive, and permanent dysfunctions.

Congenital Pyloric Stenosis, D. E. Robertson, Toronto, Canada.—A review of 450 cases was presented; 80 per cent were male; the majority were first-born; four were maternal twins; all were cured by the Ramstedt operation. The affliction may occur in only one of fraternal twins, but it is always present in both identical twins. This is strong evidence that the lesion is congenital. The preponderance of males was explained upon the basis that males from inception are more vulnerable than females. Preoperative preparation to restore fluids, sugars, and protein with fluids and blood is very important. The stomach should be emptied with a catheter immediately before operation. The pylorus has been approached through a gridiron incision just below the costal margin and to the right of the border of the right rectus. The liver which prevents evisceration is retracted upward, exposing the pyloric tumor immediately under the wound.

William E. Ladd, Boston, reported 765 cases with a mortality of 0.56 per cent in the last 177. Feeding should be started immediately after operation. Albert O. Singleton, Galveston, Tex., feels that by incising the posterior sheath of the rectus transversely through a high muscle-splitting incision evisceration can be prevented. Edward J. Donovan, New York City, reported that in 450 personal cases there had been only 1 death. If necessary two or three days should be spent in preoperative preparation with fluids and blood transfusions. Edwin M. Miller, Chicago, showed sections through the pylorus of a baby who died six months after a Ramstedt operation in which the site of section could not be identified. The thickness of the wall was fairly normal and was equal throughout the circumference. Warren Cole, Chicago, starts feeding immediately after operation. Local anesthesia is adequate. Administration of vitamin C and the use of fine silk sutures aid wound healing. Walter E. Lee, Philadelphia, noted that buried sutures disturb wound healing. Better wounds are obtained by approximating all layers with a single series of through-and-through sutures of silk.

Gastric Acidity Before and After Operative Procedure With Special Reference to the Role of the Pylorus and Antrum: A Preliminary Report of a Clinical and Experimental Study, Owen H. Wangenstein (by invitation), Richard L. Varco, Lyle Hay, Benedict Trach, and Stewart Walpole, Minneapolis, Minn.—Studies of gastric acidity were made in patients with ulcer before and after various types of gastric resections and of animals with different types of pouches. It was concluded that the stomach could be rendered achlorhydric by resection of the distal 66 to 80 per cent of the stomach. Gastric analyses made a year or more after such resections showed persistence of achlorhydria. Rapid emptying of the stomach reduces gastric acidity by reducing the gastric phase of stimulation of the secretion of hydrochloric acid.

In discussion Lester R. Dragstedt, Chicago, noted that postoperative achlorhydria gives optimum insurance against recurrence of ulcer. Roscoe B. Graham, Toronto, Canada, stated that the majority of ulcers should be treated by gastric

In discussion **Owen H. Wangensteen**, Minneapolis, Minn., noted that the incidence of leakage along gastrointestinal suture lines in animals has been greatly reduced by the topical application of crystals of sulfanilamide.

Kellogg Speed, Chicago, discussed the direct application of sulfanilamide, which has proved very effective in the treatment of infected wounds as well as an effective agent in preventing infection in noninfected contaminated wounds. It promises to be valuable in the treatment of infections of bones and joints.

Frank L. Meleney, New York City, pointed out that Key's studies were concerned with a single microorganism. Most contaminated or infected wounds contain two or more microorganisms which may present quite a different problem.

J. Dewey Bisgard, Omaha, Neb., stated that from a similar group of studies he found that sulfanilamide did not alter the normal rate or quality of healing of either soft tissue or bone.

The Rate of Healing of Tendons: An Experimental Study of Tensile Strength, **Michael L. Mason** and (by invitation) **Harvey S. Allen**, Chicago.—The flexor carpi ulnaris and extensor carpi radialis tendons of dogs were divided and immediately sutured. Tests of tensile strength of the union showed an initial drop below that of the suture in the fresh tendon. With uninterrupted and unrestricted function of the ends of the tendon separated several millimeters with partial tearing out of sutures. With restricted motion from the beginning there was less separation but there developed a large bulbous mass of fibrous tissue around the site of union. In tendons in which casting permitted no motion union took place with no separation and after fourteen days the union was sufficiently strong to withstand limited function without giving. After fourteen days the union showed a progressive loss in strength in the absence of function and a progressive increase with function. Both physiologically and histologically the most ideal unions were effected in tendons given complete rest for fourteen days; then limited function followed in 4 weeks by complete function. These results conform to the laws of healing determined by Carrel, Harvey, and others.

In discussion **Samuel C. Harvey**, New Haven, Conn., noted that in the process of wound healing there is a local reversion to embryonic tissues which are sensitive to stress. As the scar matures it adjusts itself to meet stress.

The Effects of Pressure on Tissues: An Experimental Study of the Effects of Temperature on the Survival of Anemic Tissues, **Barney Brooks** and (by invitation) **George W. Duncan**, Nashville, Tenn.—Tails of rats were rendered ischemic by applying constriction at a pressure of 130 mm. Hg around their proximal ends. These ischemic tails subjected to an environmental temperature of 40° C. for three hours became necrotic but survived ischemia for periods longer than ninety-six hours in an environmental temperature of 1° C. The survival periods at temperatures ranging between these extremes varied proportionately. Although refrigeration prevented necrosis of the ischemic tissue, the tissues showed degenerative changes.

Norman E. Freeman, Philadelphia, discussed the rapid increase in blood flow and in tissue metabolism as temperatures are raised above 34° C.

Further Anesthesia Studies With Photoelectric Oxyhemoglobinograph, **Frank W. Hartman** (by invitation) and **Roy D. McClure**, Detroit.—"Through the work of Kurt Kramer in 1933 and 1934 the measurement of oxyhemoglobin in the circulating blood was first accomplished. The method involves the isolation of an artery and the direct application of a photoelectric cell." This precludes its clinical use. Under the direction of the authors an oxyhemoglobinograph has been devised by which a continuous record of the oxyhemoglobin of circulating

upper extremity. Our present technique, intraspinal (intraarachnoid) anterior root section of D2 and D3 and trunk section below D3, gives promise of being a satisfactory solution of the problem." In an effort to prevent regeneration the sectioned trunk is ensheathed in a silk bag. Intercostal nerves 2 and 3 are also sectioned.

In discussion Peter Heinbecker, St. Louis, stated that there is good evidence that vasospastic disease is an intrinsic disease of the walls of the blood vessels and not primarily a disease of the sympathetic nervous system. Recurrence of symptoms may be explained upon this basis rather than regeneration. There is also good evidence that D1 does not carry vasoconstrictor fibers for the arm.

James C. White, Boston, noted that it has been shown that sympathetic fibers regenerate rapidly and that in the monkey section of D1 alters the temperature of the extremity.

REVIEW OF THE SECTION ON SURGERY OF THE AMERICAN MEDICAL ASSOCIATION

WOOLFOLK BARROW, M.D., LEXINGTON, KY.

AT THE annual meeting of the Section on Surgery, General and Abdominal, of the American Medical Association in New York City on June 12, 13, and 14, Edwin M. Miller and E. H. Fell, Chicago, Ill., and Clayton E. Brock, St. Louis, reported a summary of *The Treatment of Acute Appendicitis and Its Complications in Children*, based on their experience with over 1,000 cases of acute appendicitis in children. They divided these patients into three groups. In the first group of patients the inflammatory changes were limited to the appendix itself. In these patients with "obvious acute appendicitis without perforation, there is no difference of opinion about the proper treatment." There were 629 patients in this group treated by immediate operation with no deaths.

Those patients "with obvious perforation with an adequate defensive mechanism" were placed in Group 2. In this group the symptoms were usually of longer duration than in Group 1, but the patients did not seem critically ill. A mass of variable size and position was usually present due to a slow leak in the appendix with adequate defensive measures on the part of the body. In this group of patients Miller, Fell, and Brock found that conservative measures, where possible, have given the most satisfactory results. In 11 per cent of these patients surgical interference became necessary; spontaneous resolution occurred in 89 per cent. Appendectomy during the quiescent stage was urged in every instance. The mortality rate in this group of patients was 2 per cent where conservative measures were employed.

In Group 3 the patients were critically ill; there were signs and symptoms of generalized peritonitis in association with an open perforation of the appendix. Many of these were associated with obstruction to the appendical lumen. In these patients (children) conservative measures were associated with a mortality of 80 per cent. Immediate operation was associated with a mortality of 12 per cent.

Edward S. Stafford and David H. Sprong, Jr., Baltimore, presented *An Analysis of the Mortality Resulting From Acute Appendicitis*. In 1,317 consecutive patients with acute appendicitis there were 48 deaths. Prompt surgical interference was undertaken in every instance, but the essayists were careful to point out that time spent in preoperative preparation by intravenous fluid, electrolytes and blood, in their opinion, was time well spent. They considered the details of

resection and the resections should be extensive. J. Shelton Horsley, Richmond, Va., feels there is good reason to believe that after resection, regardless of extent, the remaining acid secreting glands undergo hyperplasia.

The Surgical Management of Carcinoma of the Left Half of the Colon, Howard C. Naffziger and (by invitation) H. Glenn Bell, San Francisco.—In a series of 161 cases of carcinoma of the left half of the colon (rectum excluded) major surgery was performed in 74, an operability of 46 per cent. Resections were done in 49 cases with a loss of 5 (10 per cent); 4 died of peritonitis. Types of operations used were Mikulicz, obstructive resections, Hartmann, and direct immediate side-to-side and end-to-end anastomoses. The immediate end-to-end anastomosis with preliminary cecostomy is preferred. Preoperative preparation consists, in addition to blood transfusions when indicated, of a low residue diet and one ounce of epsom salts each morning for several days. If a preliminary cecostomy has been performed, the bowel is lavaged daily.

When doing an immediate anastomosis John A. Wolfer, Chicago, has painted the cut ends of the bowel with 5 per cent phenol followed by 90 per cent alcohol. Decompression of the bowel by cecostomy or by continuous gastric suction is important. Preoperative nutritional preparation should include vitamin C (1,000 mg. of scorbutic acid daily).

The Repair of Inguinal Hernia With Transplantation of the Cord to the Femoral Canal, William F. MacFee, New York City.—By this technique the inguinal ligament is detached from its insertion in the pubic spine and freed along the superior pubic ramus until the femoral canal is unroofed. The cord is then transferred from the inguinal canal to the femoral canal and the inguinal ligament is repositioned and made fast with silk sutures which are also used to repair the floor of the canal. The operation permits complete closure of the inguinal canal without sacrificing the cord and testicle.

Following this operation in 19 cases there have been 6, or 30 per cent, recurrences. The operation was primary in 12 cases with 5 recurrences, secondary in 7 recurrent cases with 1 recurrence. Three recurred along the femoral canal.

William E. Gallie, Toronto, Canada, noted that a well-secured tense inguinal ligament is very essential for anchorage in the repair of hernia. The merits of living sutures of fascia in repair were alluded to.

Motor and Sensory Innervation of the Colon and Bladder, James C. White and (by invitation) Max Verlot and Otto Ehrenthel, Boston.—Reported were the results of an investigation of physiologic changes in the bladder and colon which follow disease, injury, or operative lesions of the brain, spinal cord, cauda equina, and pelvic nerves. The bladder was studied by means of cystometrograms and the colon by colonometrograms. The latter procedure registers the response of the colon to distention with fluid. Subjective sensations resulting from distention of both bladder and colon were also observed. Case records of increased and decreased tonus of these organs and the diagnostic significance of these determinations were demonstrated.

This method of study, according to Peter Heinbecker, St. Louis, should aid in determining the effect of functional as well as organic neurogenic disturbances upon the colon.

The Problem of Producing Complete and Lasting Sympathetic Denervation of the Upper Extremity by Preganglionic Section, Reginald H. Smithwick, Boston.—“Because we found the clinical results of postganglionic sympathetic denervation of the upper extremity to be unsatisfactory and because we found the results of preganglionic sympathetic denervation of the lower extremity to be satisfactory we have been trying to develop a technique for preganglionic denervation of the

treatment of these patients along physiologic lines, which may demand considerably more surgical skill and judgment than treatment by immediate operation.

E. H. Fell, Chicago, suggested that a palpable intra-abdominal mass felt soon after the onset of symptoms might be composed of an acutely inflamed unruptured appendix surrounded by omentum, rather than an appendiceal abscess. Appendectomy is the procedure of choice. He emphasized the importance of adequate preoperative preparation in patients with acute appendicitis. Late in the disease sufficient immunity has been established to permit a relatively satisfactory prognosis in patients in whom late operation becomes necessary.

Harvey Stone, Baltimore, repeated that there is no controversy about the handling of patients with simple acute appendicitis by prompt appendectomy. In his opinion, the improvement in the prognosis for the patient with appendiceal peritonitis was due to better treatment along physiologic lines rather than to any special surgical technique in the acute stages or to a delay in operation. Where conservative measures had been employed, Stone strongly advocated the removal of the appendix in the interval between attacks, removing it before the patient left the hospital if it seemed unlikely that it would be accomplished otherwise.

Shelton Horsley, Jr., Richmond, Va., reported a very low mortality in patients (private) with acute appendicitis. He believed this to be due to their policy of immediate operation regardless of the stage of the disease, use of the McBurney incision, removal of purulent material by suction, no intraperitoneal drainage, and simple ligation of the stump of the appendix.

John C. Gilbride, Philadelphia, reported 3 patients in whom the acutely inflamed appendix was adherent to the bladder, producing symptoms suggestive of genitourinary tract disease rather than acute appendicitis. E. H. Miller, Chicago, reiterated the importance of noninterference with localized processes.

Charles C. Lund and John H. Crandon, Boston, reported on *Experimental Scurvy and Ascorbic Acid Deficiency in Surgical Patients*. They found that the blood level of vitamin C will decrease by one-half following an average laparotomy, but will rise rapidly to preoperative levels with an adequate intake of this substance. There was no demonstrable difference in the incidence of pulmonary complications in patients with low and with normal vitamin C levels.

In the normal human experimental subject the absence of vitamin C in the diet is followed by a rapid reduction in the amount of this substance in the blood. Although the level of reduced ascorbic acid in the blood reached zero in the experimental subject in six weeks, no clinical changes were noted for four and one-half months, when a papular eruption associated with ingrowing hairs was noted. A surgical incision made three months after the beginning of the experiment healed satisfactorily and promptly. At the end of five months of vitamin C deprivation, petechial hemorrhages began to appear on the lower part of the legs. At the end of six months a surgical incision made on the back failed entirely to heal. On microscopic study of a section taken from the line of incision there was almost complete absence of intercellular substance. Following the administration of vitamin C there was prompt healing.

In routine determination of preoperative vitamin C levels, Lund and Crandon found many patients with subnormal ascorbic acid blood levels. This was frequently associated with other deficiencies, particularly hypoproteinemia. Where vitamin C deficiencies exist, they advise the administration of 1 to 4 Gm. of ascorbic acid either by mouth or intravenously.

John B. Hartzell, James M. Winfield, and J. Logan Irvin, Detroit, in their report on *Plasma Vitamin C and Serum Protein Levels in Wound Disruption* noted that most wound disruptions occur from the fifth to the tenth postoperative day. Poor operative technique, increased intra-abdominal tension, and poor general

surgical technique as of less importance than the details of postoperative care. Inadequate postoperative care was responsible for more deaths than generalized peritonitis per se. In their opinion, it is difficult to determine what patients might be expected to be benefited by conservative measures except by operation, and all patients with acute appendicitis in their care have been operated upon immediately. They report no mortality in patients with acute appendicitis without perforation, a mortality of 7 plus per cent in patients with acute appendicitis and localized abscess, and a mortality of 14.2 per cent in patients with acute appendicitis and generalized peritonitis.

Woolfolk Barrow, Lexington, Ky., and Alton Ochsner, New Orleans, presented a paper on the Treatment of Appendical Peritonitis based on their experience with 1,039 consecutive patients with acute appendicitis seen at the Charity Hospital in New Orleans. Of this number, 179 had peritonitis of appendical origin at the time of entry to the hospital.

Ten patients who either died within twelve hours of entry or in whom an incorrect diagnosis was made and incorrect treatment carried out on nonsurgical wards were excluded from detailed analysis but not from computation of the gross mortality rate. Of 15 patients with appendical peritonitis entering the hospital within twenty-four hours of the onset of their disease, 12 were treated by immediate operation with 2 deaths; 3 were treated by conservative measures with 2 deaths. Of the 92 patients with appendical peritonitis entering the hospital from twenty-four to seventy-two hours after the onset of symptoms, 61 were treated by conservative measures with 5 deaths. In the 62 patients with appendical peritonitis entering the hospital more than seventy-two hours after onset, 21 were treated by immediate appendectomy with 10 deaths; 41 patients were treated by conservative measures with 3 deaths. Generalized abdominal pain and tenderness, rebound tenderness on the left on palpation of the left side of the abdomen, absent peristalsis on auscultation of the abdomen and distention in the patient with acute appendicitis are considered very suggestive of appendical peritonitis. If, however, the least doubt persisted about the diagnosis of acute appendicitis or the presence or absence of peritonitis, Barrow and Ochsner urged exploratory laparotomy.

In the conservative management of patients with appendical peritonitis, Barrow and Ochsner believed the following procedures based on the disturbances of physiologic function which constantly occur must be carried out in great detail: elevation of the head of the bed to favor localization of residual abscesses, if any, in the pelvis; no food by mouth, either liquid or solid, to allow complete functional rest of the gastrointestinal tract; inhalation of concentrated oxygen and constant suction of gastrointestinal contents either through a Jutte, Levine, or Miller-Abbott tube to combat distention; morphine in liberal dosage at regular intervals, both for its sedative effect on the patient and its tonic action on the intestine; infusions twice daily to supply necessary fluid and electrolytes; multiple transfusions and adrenal cortex extract for their tonic effect on the patient; sulfanilamide as an 0.8 per cent subcutaneous infusion to combat infection, and careful and repeated search for, and appropriate treatment of, residual abscesses. The locations of these residual abscesses were listed in the order of their frequency as occurring in the right iliac fossa, in the cul-de-sac, or pouch of Douglas, in the left iliac fossa, in the subhepatic space, in the subdiaphragmatic space, and in the liver following pyelophlebitis.

In the discussion of this symposium on appendicitis, Ochsner noted that "there was no conservative treatment of acute unperforated appendicitis." Prompt appendectomy is the only procedure of choice. In his opinion conservative measures in the treatment of appendical peritonitis should be limited to those patients with localization or beginning localization of their infection. In the treatment of these patients, Ochsner re-emphasized the importance of full and adequate

indication for exploratory laparotomy. The signs and symptoms of surgical shock were exhibited not infrequently. Dullness in the flanks was found occasionally. The temperature was usually normal or subnormal immediately after injury, but, should inflammation occur, it might become elevated. The prognosis in these patients was influenced by the nature and the extent of the traumatizing force; by the nature and extent of associated injuries, both intraperitoneal and extraperitoneal, as well as the interval between injury and operation. They advocated the use of through-and-through sutures in the closure of the abdominal wall in these patients.

In the discussion of the two preceding papers, Adolph A. Walkling, Philadelphia, stressed the importance of a blood bank in permitting early transfusion, as well as the importance of thorough exploration in patients with penetrating gunshot wounds of the abdomen. He felt that the more rapidly preparations for operation could be carried out, the better the prognosis for the patient. In the experience of Walkling, the mortality had been 93.7 per cent where exploratory laparotomy had not been done and 50 per cent in those patients treated by surgical exploration of the abdominal cavity.

Walter E. Lee, Philadelphia, noted that a gunshot wound of the abdomen was, by and large, the most effective known way of committing homicide and was becoming even more fatal due to the higher velocity of the bullets. Lee considered the interval between injury and operation to be of great prognostic importance.

Thomas M. Joyce, Portland, Ore., emphasized the importance of early and repeated blood transfusions and noted that a blood bank made this much easier to accomplish. Overlong operative procedure had been associated with a rise in mortality rate. In patients with suspected subcutaneous wounds of the abdomen, Joyce advocated early exploratory laparotomy where the slightest doubt persisted rather than waiting until a time when surgical intervention would be of little avail.

Rettig A. Griswold, Louisville, Ky., advocated prompt operation in patients with gunshot wounds of the abdomen whether the patient was in shock or not. Where shock was present, it was usually due to massive intraperitoneal hemorrhage which is better treated by surgical hemostasis than by supportive measures. Griswold doubted the wisdom of celiotomy in patients with iecpiek or shotgun wounds of the abdomen, for in iecpiek wounds or shotgun wounds from a distance perforations in the gastrointestinal tract become sealed spontaneously. In shotgun wounds of the abdomen inflicted at close range, such large defects were made in the continuity of the gastrointestinal tract that operation could accomplish little.

Leo Eloesser, San Francisco, believes that many patients with gunshot wounds of the abdomen will die regardless of the type of treatment instituted. He advocated the more frequent use of enterostomy, colostomy, and gauze packing in desperately ill patients.

Harry E. Mock, Chicago, cautioned against allowing the presence of an obvious head injury to conceal associated abdominal injuries. Mock also reported 2 patients in whom traumatic rupture of the colon was caused by compressed air, introduced into the anus as a practical joke.

J. Norman O'Neill, Los Angeles, noted that traumatic rupture of the liver in automobile accidents was not uncommon and that in many of these patients the associated hemorrhage would cease spontaneously. Spontaneous rupture of the stomach, though rare, had also been observed.

Rippy, in closing, stated that the mortality in gunshot wounds of the abdomen was lowered by early operation, blood transfusions, and the minimum amount of surgery necessary under the circumstances. Sulfanilamide was considered to be of limited value.

condition of the patient, particularly where there was a low ascorbic acid blood level and hypoproteinemia, were associated with an increased tendency to wound disruption. Subclinical scurvy was found not uncommonly in patients whom they studied. Experimentally in the dog, low vitamin C intake and hypoproteinemia produced by plasmapheresis were associated with a much higher incidence of wound disruption than in controls. Vitamin C requirements are increased by infection. Sulfanilamide affects the blood level of vitamin C adversely.

In 20 patients with wound disruption studied by the essayists in 1939, the blood levels of vitamin C and plasma protein were below normal. Of these patients, the great majority had had operations upon the stomach or for malignant disease. Three per cent of the patients entering the Detroit Receiving Hospital with a perforated peptic ulcer had wound disruption.

In the discussion of the two preceding papers, Thomas Mackie, New York City, emphasized the importance of the entire nutritional state of the patient rather than any one single factor in wound healing. A subnormal blood level of ascorbic acid does not necessarily indicate scurvy nor is it inevitably associated with an increased incidence of postoperative complications. A low ascorbic acid blood level, however, should be viewed as a danger signal for it is commonly associated with other nutritional deficiencies, all of which should be corrected rather than a single one.

J. E. Rhoades, Philadelphia, noted that in experimental protein deprivation there was very little tendency to fibroblastic proliferation in experimental wounds. He suggests three possible mechanisms which might be responsible for this lack of fibroblasts: local edema due to loss of plasma colloid osmotic pressure; interference with nutrition by exhaustion of the labile protein store or by interference with the circulation. The administration of acacia to experimental animals with a low plasma protein helped somewhat, presumably due to the relief of edema.

Marshall Bartlett, Boston, emphasized the length of time during which the plasma vitamin C level was zero before clinical scurvy developed.

Charles C. Lund suggested that sufficient vitamin C depletion to be solely responsible for failure to wound healing is rare. In such a depleted subject, however, vitamin C alone was responsible for a return to normal. Adequate surgical technique continues to be important.

Elkin L. Rippey, Nashville, Tenn., in a review of 292 Perforating Gunshot Wounds of the Abdomen found that the incidence had increased in the past fifty-one years. Of 24 patients in whom abdominal exploration was not done, 23 died. In those patients in whom exploratory laparotomy revealed perforation of a viscus, the mortality was 61.9 per cent. The mortality increased with increasing age and was higher in colored than in white patients. The sooner after injury operation was performed, the lower the mortality. The mortality increased in proportion to the amount of hemorrhage and the greatest single cause of death was shock and hemorrhage. Injury to the colon was associated with a poorer prognosis than was injury to any other viscus. Patients in whom the duration of operation was between one hour and one and one-half hours on the average had a better prognosis than those in whom surgical procedures were completed in less than one hour or were prolonged beyond one and one-half hours. Failure to close one or more perforations was responsible for death in several instances.

Harold Price Totten and J. N. O'Neill, Los Angeles, presented a paper on Subcutaneous Injuries of the Abdomen. They found the diagnosis impossible to make unless such a condition is suspected. The usual clinical signs and symptoms associated with injuries to the liver, spleen, intestine, mesentery, and urinary bladder were considered in detail. Abdominal pain was the most constant single symptom and this, when associated with a mounting pulse rate, was considered sufficient

died. There was residual impairment in function in many more. Early radical débridement was urged, followed by either local or systemic exhibition of sulfanilamide. Débridement was also carried out in old injuries.

In the discussion of this paper, Michael L. Mason, Chicago, noticed that such injuries are becoming more frequent. In superficial injuries the prognosis is good under conservative management. In deeper injuries there is usually much dead and devitalized material which should be removed. He does not favor cauterization of the tissues with chemicals or the electrosurgical unit. The lacerations are left widely open. In such injuries, coming for medical attention some time after their injury, débridement is followed by the liberal application of zinc peroxide, splinting of the injured member, and bed rest. Conservatism was advocated in the treatment of involved bones and joints.

Frank E. Meleney, New York City, said that fusiform bacteria, anaerobic and aerobic hemolytic streptococci, and spirochetes were found in such injuries and that under treatment the nonhemolytic bacteria disappeared first, followed by the fusiform organisms. The spirochetes were the last to leave. Zinc peroxide had been much more effective in the control of these organisms than arsphenamine. He urged repeated aerobic and anaerobic cultures to help evaluate the clinical course of these patients.

Claude E. Welch, Boston, urged early immediate drainage in these patients except in the presence of spreading lymphangitis. In early cases electrocautery excision of the injured area had been found satisfactory. In 31 patients with human bite infections seen at the Massachusetts General Hospital, the injury was at the metacarpophalangeal joint in 18. Four of these patients required an amputation.

In conclusion Boland emphasized the importance of knowing the usual route of spread of infection and of alertness in treating such complications as might arise.

Thomas M. Joyce, Portland, Ore., in his Chairman's Address, *Combination of Old and New Methods in Repair of Inguinal Hernia*, gave an interesting historical review of the surgical treatment of hernia, noting that the injection treatment of hernia is at least 150 years old and that until recently surgery has been considered a last resort. Following the development of anatomic dissection and repair of hernia by Bassini and Halstead, McArthur suggested the use of a strip of fascia taken from the aponeurosis of the external oblique to reinforce the suture line. Kirschner proposed the use of a transplant of fascia. Gallie suggested the use of sutures of fascial strips taken from the thigh and later the use of a many tailed fascial graft. Wangenstein suggested the use of an iliotibial fascial graft.

Joyce advocated the routine use of fascial strips obtained either from adjacent fascia or from the thigh, and felt that this was particularly indicated in direct inguinal, ventral, or recurrent hernias. He advocated the suture of fascia to fascia for, when muscle was sutured to fascia, satisfactory union was unlikely. He reported 184 personal cases in which fascial strips had been used with but a single recurrence. Local anesthesia was not used. In 3 patients in whom wound infection developed, the fascia did not slough out.

Carrington Williams and Paul Kimmelstiel, Richmond, Va., reported 8 patients with *Syphilis of the Stomach*. In all of these patients ulceration occurred in the region of the pylorus secondary to an infiltrating lesion in the submucosa. The signs and symptoms are suggestive of carcinoma of the stomach. Roentgen-ray examination shows a funnel deformity of the lower end of the stomach. This is only suggestive, not pathognomonic. On gross examination the ulcerated area is usually smaller than the x-ray would have led one to suspect. The tributary lymph nodes are enlarged. On microscopic examination, there is diffuse round-

Reed M. Nesbit and Rigdon K. Ratliff, Ann Arbor, Mich., in their report on **Hypertension Associated With Unilateral Kidney Infection** stated that hypertension had been shown both experimentally and clinically to be associated with unilateral or bilateral damage to the kidneys in certain instances. Patients in whom there is renal damage account for the largest group of therapeutic failures following neurosurgical operations. Two patients were reported with hypertension and occlusion of one renal artery. In these patients symptomatic relief followed nephrectomy. Traumatic injury to the kidney with the production of a parenchymal infarct or urinary obstruction and ischemia due to obliteration of the parenchymal blood supply may have the same effect. In 6 of 10 patients with unilateral chronic pyelonephritis and hypertension, there was improvement following unilateral nephrectomy. On pathologic examination of these kidneys, arteriolar thickening was found. In the authors' opinion, chronic infection was the most frequent etiologic agent producing unilateral kidney damage associated with hypertension. Nesbit and Ratliff caution that hypertension does not always follow damage to kidneys and that, if a patient has renal damage and hypertension, it does not of necessity follow that the former is responsible for the latter.

In the discussion of this paper, E. Granville Crabtree, Boston, noted that, in his opinion, hypertension will eventually be considered as the end result of pathology elsewhere. It has been known to result from unilateral kidney damage within six months. In many instances, however, histologic changes may be found in the kidney in the absence of hypertension.

Henry A. Schroeder, New York City, stated that, in his opinion, there were two factors responsible for hypertension in patients with unilateral kidney disease, one renal, the other constitutional in nature. And that, although regression of hypertension might follow nephrectomy, the patient was still a potential hypertensive and the relief might be only temporary.

George W. Fish, New York City, suggested that the renal arteriolar lesions might be the result rather than the cause of hypertension. The best therapeutic results from unilateral nephrectomy have been obtained when the hypertension is of less than two years' duration. He reported a patient who had died from a pulmonary embolus following unilateral nephrectomy in a patient with unilateral renal disease and hypertension. Although the patient's hypertension had been lowered, autopsy showed that arteriolar damage had already occurred in the remaining kidney. He expressed the hope that a substance could be found to neutralize the pressor substances released by damage to the kidney parenchyma.

In closing, Nesbit said that all the patients considered here had entered the hospital with the diagnosis of essential hypertension. There was nothing in the patient's history to suggest an organic lesion. In patients on the urologic service the incidence of hypertension is low.

Frank E. Boland, Atlanta, Ga., presented a paper on **Morsus Humanis**. Human bite infection occurs in two ways, one by striking the teeth of an opponent with the knuckles, the other as the victim of a bite. Except on the hands or fingers, the results of human bites were similar to the result of injuries from other agents. In human bite injuries to the knuckles serious infections and unfortunate sequelae were not uncommon due to violent dissolution of tissues, virulent bacteria, spread by the gliding action of tendons, and the difficulty of cleaning the joint and its capsule. In this group of patients bites inflicted by negroes were more serious than those inflicted by white people and in Boland's experience were becoming even more virulent. The bite of the blue-gummed negro was no more fatal than that of any other negro. From observations on the teeth of dogs, Boland concluded that the type of diet had much to do with the bacterial flora of the teeth. In 17 human bite injuries to the hand osteomyelitis developed in 6. One patient lost a phalanx, 2 an entire finger, 1 the entire thumb and forefinger, and 1 patient

sel; eighth, ulceration in the suture line; ninth, hypoproteinemia with edema and impaired motility. Hoag and Saunders proposed anastomosis of the afferent and efferent loops of jejunum beginning at the point of anastomosis with the stomach. In several patients in whom the procedure had been used, satisfactory results were obtained.

In the discussion of these papers, Alton Ochsner, New Orleans, emphasized the importance of suspecting carcinoma in the stomach in patients with vague abdominal complaints. In 6 patients with carcinoma of the stomach seen in the Charity Hospital of New Orleans, previous appendectomy had been performed elsewhere through a buttonhole incision for vague abdominal symptoms. Two per cent of all autopsies performed at the Charity Hospital were done on patients with carcinoma of the stomach. Ochsner emphasized the importance of the clinical investigation of Julius Bauer in which it was shown that individuals whose families had a high incidence of benign peptic ulceration as well as gastric carcinoma were particularly likely to develop a gastric malignancy. The importance of this is that patients with a benign lesion of the stomach in whose family history there is a frequency of peptic ulceration should have a subtotal gastric resection because of the greater likelihood of this ulcer's becoming malignant than that in an individual whose family history is negative for gastric disease.

William Barclay Parsons, New York City, felt that the presence of any gastric ulceration should be regarded as highly suggestive of cancer. The gastroscope may be of some value in establishing the character of these lesions.

Arthur W. Allen, Boston, noted that better preoperative preparation, better technique, better selection of the type of operation used, and a more adequate knowledge of biochemical disturbances were all permitting more extensive surgery on patients with gastric lesions than had ever been possible before. In patients developing obstruction following gastroenterostomy or gastric resection, marked inflammatory changes occur around the site of anastomosis (an observation emphasized later by Howard K. Gray) and, although jejunoplasty may be possible, it is a major surgical procedure. The simpler operation of jejunostomy will permit adequate nutrition of the patient while the inflammation surrounding the malfunctioning stoma subsides, allowing the re-establishment of function through the original stoma. Five patients in whom this complication occurred were treated by jejunostomy with satisfactory results. In one instance feeding through the jejunostomy tube was necessary for thirty-five days.

John H. Powers, Cooperstown, N. Y., in an analysis of 500 Automobile Accidents in a Rural Area Traversed by a Transcontinental Highway found that they occurred most frequently during the summer months in clear weather on dry hard roads during daylight hours. Powers believed that excessive speed, a lack of knowledge of the usual hazards of the highway, and unfamiliarity with the territory traversed were responsible for the majority of these. The mortality in this series of patients was 8.5 per cent.

In the discussion of this paper, Alan DeF. Smith, New York City, believed that it was the reckless driver who was largely responsible for automobile accidents, but the innocent driver was no less apt to suffer. In his opinion revocation of driving licenses should be more frequent, and perhaps licenses should not be issued at all to minors. He further advocated compulsory insurance to defray hospital and medical expenses of injured persons.

Powers, in closing, suggested that 95 per cent of all highway accidents were due to negligence and were preventable. Of 712 patients admitted to the Mary Imogene Bassett Hospital, 73 per cent paid in full, 12 per cent in part, and 15 per cent made no payment whatsoever, the latter representing a loss of over \$20,000 to the hospital.

cell infiltration. True gummas with or without giant cells may occur. Proliferative endarteritis occurs, but it is not specific to syphilis of the stomach. The walls of the veins seem to be encroached upon with destruction of the elastica and obliteration of the lumen. Spirochetes are not usually found nor can syphilis be produced by the intratesticular injection of this material into rabbits. The diagnosis must be made upon the history, clinical findings, and serology as well as the pathology. In 6 patients resection of the pylorus was accomplished without a fatality. One patient died at a subsequent date from massive hemorrhage; 3 have remained well; and 2 have been lost to follow-up.

Karl A. Meyer, Chicago, in the discussion of the above paper said that he believed the incidence of syphilis of the stomach was increasing. The outstanding clinical phenomenon is a gradual decrease in the capacity of the stomach. Diagnosis upon x-ray evidence alone is unsatisfactory. Spirochetes when found in the stomach may be Vincent's organisms rather than *Spirochaeta pallida*.

In a report on Cancer of the Stomach With Particular Reference to the Significance of Persistent Symptoms Ascribed to the Stomach and the Malignant Potentiality of Gastric Ulcers, Howard K. Gray, Rochester, Minn., noted that two and one-half times as many people had died of cancer of the stomach in the past fifteen years as in all the wars in which this country had been engaged. He emphasized that the signs and symptoms of carcinoma of the stomach were frequently vague and indefinite until the tumor had become so large that successful therapy was no longer possible. Gastric carcinoma may be suggested by symptoms similar to those of a peptic ulcer, by vague and indefinite abdominal complaints, by gradual loss of weight over a prolonged period (unexplained hypochromic anemia), or by a sudden massive hemorrhage. The appearance of the symptoms of carcinoma of the stomach usually included in textbooks generally indicates an advanced and incurable carcinoma of the stomach.

In one-third of the patients with carcinoma of the stomach observed by Gray there had been a "typical" history of peptic ulcer; in three-fourths there had been persistent symptoms without remission; in one-fourth the symptoms had persisted for more than a year. In one-fourth of these patients there had been a change in type in gastrointestinal symptoms of long standing. In some patients there were no symptoms referable to the gastrointestinal tract.

In three-fourths of the patients seen with supposed benign gastric ulcers, immediate operation was advised. In the remaining one-fourth hospitalization and continuous observation were urged. Although even in patients with carcinoma of the stomach ulcer niches have been known to disappear, prompt disappearance of a gastric ulcer under conservative measures is strong evidence against carcinoma.

In patients with carcinoma of the stomach, 50 per cent were deemed inoperable at the time of observation. In 25 per cent of those patients resection was possible; 30 per cent of these survived five or more years. Only the surgeon can offer any hope to the patient with carcinoma of the stomach.

Carl T. Hoag and John B. deC. M. Saunders, San Francisco, urged Jejunoplasty for Obstruction Following Gastroenterostomy or Subtotal Gastric Resection if relief does not follow a not too long period of conservative treatment. They listed the most frequent causes of obstruction in these patients as: first, an improperly placed stoma; second, too small a stoma, a complication more frequent when placed stoma; third, insufficient allowance is made for contraction of a previously dilated stomach; fourth, too short a proximal loop of intestine by traction and rotation or too long a loop by distention; fifth, inadequate fixation of the stomach to the mesocolon with subsequent herniation; sixth, adhesions in the region of the stoma; seventh, tension on the middle colic artery when the anastomosis has been to the right of this ves-

used. In those patients developing signs of increased intracranial pressure, limitation of fluid intake to less than 1,200 c.c. daily, magnesium sulfate by mouth or enemas, the intravenous injection of hypertonic glucose or sucrose, and lumbar puncture were advocated.

Operative interference was limited to those patients with a depressed fracture or extradural hematoma. The mortality in patients operated upon was 50 per cent.

In the discussion of this paper, **S. Bernard Wortis**, New York City, stated that in his experience conservative measures by and large had been attended with the most satisfactory results, although the treatment of each patient had to be individualized.

Donald Munro, Boston, suggested that it was impossible to present comparative statistics without an accepted and standard classification of these patients on the basis of the extent and type of injury to the brain. In the large group of patients with head injuries seen at the Boston City Hospital, there were many patients with compound fractures of the skull, which exerts a profound effect upon the mortality rate. In 2.2 per cent of the patients, extradural hematomas were encountered. Three hundred patients with subdural hematomas have been seen. Munro advocated early and thorough operation in these patients. The mortality rate was 34 per cent.

In closing, **Harold C. Voris** related that his experience with operative interference in patients with a subdural hematoma had not been a happy one.

Joseph S. Barr, Boston, reported the **Indications and Technique for Operative Treatment of Fracture of the External Tibial Condyle (Bumper Fracture)** as developed in the Fracture Clinic of the Massachusetts General Hospital. In those patients the external semilunar cartilage is usually torn in addition to the fracture of the external tibial condyle. The type of treatment indicated depends upon the degree of displacement of the external tibial condyle. Where this is less than one-half inch, good results can be anticipated from conservative measures; i.e., immobilization until the swelling subsided (aspiration of the knee joint does no harm but is usually not necessary). Weight bearing is forbidden for ten weeks and a brace is worn for from two to six months longer. Physiotherapy is used throughout the treatment.

In those patients with more than one-half inch displacement, operative replacement of the fragment is necessary to prevent hypertrophic changes in the knee joint and interference with its function and stability. When operative interference is undertaken, Barr recommends removal of the damaged semilunar cartilage and fixation of the replaced fragments by a long vitallium screw held by a nut and washer. The screws are removed at the end of a year. The average period of disability in these patients was eight months.

In the discussion of this presentation, **Carl E. Badgley**, Ann Arbor, Mich., noted that there were many types of this fracture and that there might even be posterior rather than lateral displacement of the fragments. The choice of conservative or operative treatment as well as the type of operation employed must depend upon the pathology found in the individual patient.

Carl E. McBride, Oklahoma City, noted that there were two problems in these patients, first to restore the bone architecture, and second to hold it. Even where the roentgen ray shows but little displacement, operation may be the procedure of choice for more extensive injury is frequently found by operation than shown by the x-ray.

James S. Speed and Harold B. Boyd, Memphis, Tenn., summarized their experience with 62 patients with **Fracture of the Ulna With Dislocation of the Head of the Radius (Monteggia Fracture)**. In 83 per cent of these patients there was an anterior dislocation of the radius; in 73 per cent the fracture of the ulna was in the upper third. A fracture of the ulna with angulation or displacement strongly suggests an accompanying dislocation of the head of the radius, although the latter may be difficult to determine by x-ray examination. Recognition and treatment of both lesions are important, for, if adequate correction is not obtained, arthritic changes in the elbow joint and limitation in pronation-supination are to be expected. The maintenance of adequate fixation by conservative means in such patients may be difficult or impossible. In these instances Speed and Boyd advocate operative fixation of the head of the radius by a sling of fascia obtained from the deep muscles of the arm. Approach to the head of the radius was obtained through an incision along the subcutaneous border of the ulna with reflection of the supinator and anconeus muscles. In this way no muscles are divided or split. Where the injury was of long duration, excision of the head of the radius was advised. In patients with nonunion of the ulna, an onlay bone graft was recommended.

In the discussion of this paper, **Herman F. Johnson**, Omaha, Neb., emphasized the difficulty in making a diagnosis of anterior dislocation of the elbow by roentgen-ray examination and suggested the making of x-ray plates of both elbows in these patients. He suggested the use of steel pins for fixation in compound fractures or fixation of the fragments by a Kirschner wire introduced through the olecranon process and threaded the entire length of the ulna.

Benjamin Franklin Buzby, Camden, N. J., noted that every oblique fracture of the ulna must be accompanied by a dislocation of the head of the radius. He further noted that excision of the head of the radius in adults was accompanied by but little disability, but in children it was not uncommonly followed by disturbances in growth.

G. Mosser Taylor, Los Angeles, reported a patient with a fracture of the ulna and dislocation of the radius in whom there was but 50 per cent pronation treated by conservative measures followed by five manipulations under anesthesia.

Albert Key, St. Louis, was of the opinion that satisfactory results could be obtained in a certain number of these patients by conservative measures. In compound fractures he advocated the local application of sulfanilamide. Surgical intervention in these patients requires specialized knowledge.

In closing, Boyd remarked that the power of the supinators of the forearm is enormous and makes adequate fixation by conservative measures almost impossible.

Harold C. Voris, **Adrien Verbrugghen**, and **Jerry J. Kearns**, Chicago, reviewed more than 1,400 patients with **Head Injuries** seen in the Cook County Hospital. Approximately one-fourth of these were due to automobile injuries, one-fourth to a fall, one-fourth to assault, and the remaining one-fourth to miscellaneous causes. In 80 per cent of these patients, there were associated injuries. The mortality for the entire group was 13 per cent. In the various age groups the mortality rate rose steadily with an increase in age. Forty per cent of the patients who died did not have a demonstrable fracture of the skull.

In the treatment of these patients intravenous glucose was given if they were in shock or collapse. Saline solution was not used. X-rays were deferred until it was deemed safe to take them. Morphia, particularly in the early stages, was not

sible and directed that it be made directly over the diseased tissue. He urged closure of the peritoneum in these patients without drainage.

This paper invoked a very considerable amount of discussion. **Fred R. Fairchild**, Woodland, Calif., re-emphasized the need for intestinal decompression and discussed the Miller-Abbott tube, which he said had saved the lives of 2 patients in his clinic in the preceding year. He reported a mortality rate of 1.02 per cent in 600 cases of appendicitis. **Thomas M. Joyce**, Portland, Ore., emphasized the value of the muscle-splitting operation, i.e., the McBurney incision, and reported that at times he used the Ochsner treatment without surgery. **F. L. Reichert**, San Francisco, emphasized the need for care of the tube and suggested that, if such care were neglected, tracheal stenosis might develop.

The Management of Surgical Injuries to the Ureter, **Alexander B. Hepler**, Seattle, Wash.—The author limited his discussion to the management of surgical injuries to the ureter which occur accidentally in the course of pelvic operations, and therefore are primarily the problems of the pelvic surgeon. He believes that such an injury is much more common than is usually thought. The author encountered 6 cases, 1 of which was bilateral, in his private practice in the last ten years. If the ureteral injury is recognized at the time of operation, the author advises ureteroureterostomy if possible, with an indwelling ureteral catheter leading out through the urethra. Ureterostomy should be performed above the anastomosis by feeding a small ureteral catheter from a slit in the ureter out through a stab wound in the flank. If ureteroureterostomy is not practicable, ureteroenterostomy should be done. If the accident is discovered postoperatively, ureterostomy rather than nephrostomy is the temporary procedure of choice. Later, intestinal implantation of the ureter might be done.

Frank Hinman, San Francisco, said that he could not agree that ureterostomy is better than nephrostomy. He prefers nephrostomy in cases of ureteral block at operation. He also advised the use of ureteral catheters in cases in which injury is suspected at the time of operation. He believes that the average surgeon should not attempt ureteroenterostomy when an injured ureter is found at the time of operation. He pointed out that many minor injuries of the ureters heal themselves.

A. J. Scholl, Los Angeles, suggested the use of ureteral catheters placed in the ureters before operation for extensive pelvic disease. These catheters are of tremendous aid to the surgeon in recognition of the location of the ureters, thereby permitting avoidance of them. Ligation of tissue in the region of the ureters should be done with absorbable ligatures, as their absorption may relieve an obstructed ureter. Ligatures and sutures of silk or linen would cause permanent obstruction.

Ureteral Stones, a Nonsurgical Method of Treatment, **Albert J. Scholl**, Los Angeles.—Scholl first discussed the paper of Hager, who advised the use of prostigmin for ureteral stones in the hope that the vagotonic action of this drug might increase the natural expulsive force of the ureter. The dosage is 1 c.c. of 1:2,000 solution injected subcutaneously every four hours for four doses. Its use is contraindicated in feeble patients and in those subject to asthma. The author discussed the records of several of his own patients, 7 of whom have remained in the best of health. He advised one or two series of injections in an effort to aid in expulsion of the stones before resorting to more extensive methods of manipulation or surgical removal.

W. A. Taylor, Ellensburg, Wash., who was treated by Scholl for ureteral stones, feels that morphine counteracts the effect of prostigmin and should not be used when prostigmin is employed. He finally had several doses of prostigmin and

In closing, Barr noted that traction or manipulation of the leg is without effect upon the position of the tibial condyle. Operative interference is a major surgical procedure and requires specialized technique and experience. In old fractures with union in poor position, associated with disability, the same procedure is advocated following refracture of the fragments.

Rufus H. Alldredge, New Orleans, in his paper on **Complicated Pott's Fractures Requiring Open Reduction** noted that this fracture was the result of external rotation and in some instances was associated with extensive ligamentous damage as well as a fracture of the fibula. Where this damage was sufficient to result in a widening of the ankle mortis, a painful osteoarthritis was the usual result unless this deformity was corrected. Where there was no interposition of soft parts, early accurate reposition of the fragments was not difficult and was usually followed by satisfactory function.

In certain instances, however, particularly where ligamentous structures failed to heal, there was both anteroposterior and lateral instability. Internal fixation of the fragments, particularly fixation of the lower end of the fibula to the tibia, in these patients was associated with satisfactory functional results. Operative technique was described in detail.

In the discussion of this paper, Clay Ray Murray, New York, N. Y., stated that a diastasis of the ankle mortis was of more importance to the patient than the associated fracture, and it was important to determine its presence or absence at the original examination. In his experience surgical intervention when necessary with particular attention to tight fixation of the lower end of the fibula to the tibia had been associated with good recovery of function. Weight-bearing should be avoided for at least twelve weeks when a diastasis existed.

G. E. Eaton, Baltimore, deprecated reliance upon fluoroscopic examination of patients with suspected fracture, since it was not entirely reliable.

In closing, Alldredge noted that a posterior fragment of bone, unless rather large, could be replaced satisfactorily by external pressure.

REPORT OF THE MEETING OF THE PACIFIC COAST SURGICAL ASSOCIATION, PORTLAND, ORE., APRIL 3-6, 1940

H. H. SEARLS, M.D., SAN FRANCISCO, CALIF.

President's Address, Richard B. Dillehunt, Portland, Ore.—Dillehunt discussed the problem of supplying sufficient opportunities for young graduates in medicine to fulfill the requirements which will permit them to take the examinations given by the various boards of surgery and the surgical specialties. He observed that, if a sufficient number of residencies are to be approved, many of these must be in nonteaching hospitals and that, in such case, the resident should be assigned to the outstanding surgeon of its staff rather than to the hospital, thereby making such a staff member responsible for adequate training of the resident. In his opinion, the multiplicity of boards might give way to a single high standard of requirements for Fellowship in the American College of Surgeons.

Appendicitis With Complications—Reduction of Mortality by Continuous Gastric Lavage, Robertson Ward, San Francisco.—Ward, who originated the use of continuous gastric drainage in the treatment of peritonitis and ileus, emphasized its value in the postoperative cure of the patient with acute perforative appendicitis. He advised the use of the muscle-splitting approach of McBurney when pos-

sible and directed that it be made directly over the diseased tissue. He urged closure of the peritoneum in these patients without drainage.

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described its effects on the rectum and the central nervous system. He then related the expulsion of a stone from the ureter into the bladder with such force that he felt it occur. **A. B. Hepler**, Seattle, Wash., in discussing Scholl's paper, agreed that prostigmin is of considerable value.

Umbilical Endometriosis, **Herbert S. Chapman**, Stockton, Calif.—Although apparently endorsing the Sampson theory of endometrial transplants as the etiologic factor in most cases of endometriosis, the author believes that this theory does not explain endometriosis of the umbilicus. In reviewing the literature he discovered that approximately 100 cases have been reported and concluded that endometriosis of the umbilicus no longer may be considered a rare entity.

R. E. Watkins, Portland, Ore., reported several cases. **Edmund Butler**, San Francisco, described the dangers entailed by the difficult resection of endometrial tumors in the pelvis. Because of the great likelihood of injury to the rectum, he suggested that in many instances sterilization surgically or by x-ray is a more rational procedure than excision of the tumor. **G. C. Schanffler**, Portland, Ore., reported 51 cases of endometriosis in laparotomy scars.

Tumors in Infants and Children; Conservatism in Surgical Therapy, **Clarence W. Brunkow**, Portland, Ore.—The essayist made a plea for conservatism in surgical procedures on the infant. Such conservatism consists of speeding up the operative procedure, limiting the length of operation to one hour and the loss of blood to 1 ounce. Multiple-stage procedures should be used if the operation cannot be finished within these limits. He presented a series of 115 cases of infants operated upon for congenital maldevelopment, new growths, inflammation, mechanical factors, and trauma and used this series to defend his stand for conservatism.

W. J. Norris, Los Angeles, pointed out that nearly 20 per cent of all malignant tumors in children occur in the kidney. He suggested that peritoneoscopy is of value in the diagnosis of abdominal tumors in children. **Donald Trueblood**, Seattle, advised that for hemangiomas of the skin surgery is a better method of treatment than x-ray or radium. He also emphasized the importance of multiple-stage operations and conservatism in surgery.

The Treatment of Massive Hemorrhage in Peptic Ulcer, **Caleb S. Stone, Jr.**, Seattle.—Stone reviewed the literature and reported a series of cases from the Mason Clinic. He believes that in patients under 50 years of age surgery for the control of hemorrhage is rarely indicated. In patients over that age, however, massive hemorrhage is an indication for early operation. Gastric resection is his choice of operation. Repeated transfusions to maintain blood volume must be continued throughout the preoperative period.

Otis Lamson, Seattle, was inclined to be more conservative than Stone. He reported that in his own practice he had never had a patient die of hemorrhage from a peptic ulcer. **Paul Gmby**, Seattle, pointed out that, if the patient can be tided over the first hemorrhage, x-ray studies will determine whether or not the bleeding is from an ulcer and, if an ulcer is present, where it is located. This, of course, is of great value to the surgeon.

Traumatic False Sacular Aneurysm Resulting From Erosion of the Femoral Artery in a Patient With Hereditary Deforming Chondrodysplasia, **Edmund Butler** and **Martin Debenham**, San Francisco.—Chondrodysplasia is a disease of the growth period, often resulting in characteristic deformities and the development of multiple osteochondromas. Unless located near large vessels or nerves, osteochondromas rarely are associated with symptoms. When located near a large artery, however, the pulsation of the vessel against the bone causes injury to the arterial

wall and the formation of a traumatic false aneurysm. The authors reported such a case in a young girl in whom a false aneurysm of the femoral artery developed. Relief was obtained by ligation of the femoral vessel and excision of the sac.

Cancer of the Breast, A. Aldridge Matthews, Spokane, Wash.—Matthews discussed his series of tumors of the breast, including cancer. He suggested that the modern tendency to wean babies early may be a factor in the development of carcinoma of the breast.

The Curability of Cancer of the Breast, a Ten-Year Follow-Up, Edwin I. Bartlett, San Francisco.—Bartlett reported the statistics of the University of California Hospital for operations for cancer of the breast.

These two papers were discussed by **Otis Lamson, Seattle**, who emphasized the need for thoroughness in this operation and urged that no sacrifice be made of such thoroughness even when x-ray therapy has been planned as an adjuvant. He urged radical mastectomy, even with a history of long duration and in the presence of axillary metastases if x-ray examination failed to demonstrate intrathoracic extension. **A. R. Kilgore, San Francisco, Calif.**, discussed the place of radiation therapy in cancer of the breast. He does not use such therapy for patients who have no axillary involvement. He pointed out the discomfort of a severe x-ray burn, the possibility of increased swelling of the arm from blocked lymphatics, and the added expense to the patient as reasons for seriously considering each case individually before recommending x-ray therapy.

Pulsion Diverticula of the Hypopharynx, Charles T. Sturgeon, Los Angeles.—Sturgeon reported a large series of cases and discussed their treatment.

T. M. Joyce, Portland, recommended the indwelling catheter and the one-stage operation when possible. He has had no difficulty with the recurrent laryngeal nerve in his series. **H. Glenn Bell, San Francisco, Calif.**, suggested that it is very difficult to put a tube down before operation, but very simple to place it at operation. He recommended its use, pointing out that the patient could be fed immediately. He reported the cases from the University of California Hospital.

Throughout the discussion there was much talk about single-stage and two-stage operations.

Some Unusual Tumors of the Cervical Region, Thomas M. Joyce and Frank Menne, Portland, Ore.—In this paper the authors discussed tumors of the region of the neck and face and reported cases to illustrate each type. They divided their cases into: (1) primary tumors of the salivary glands; (2) unusual tumors originating in the branchial cleft; (3) unusual tumors of thyroid and parathyroid origin; and (4) tumors of miscellaneous origin.

In their opinion nearly all such tumors originate from errors in development of the foregut.

H. H. Searls, San Francisco, pointed out in discussion that the presence of thyroid tissue outside the thyroid gland proper carries the threat of malignancy. **Brien King, Seattle**, added several cases of his own in discussion of the paper.

Team Work in the Care of the Surgical Patient, Irving Wills and Albert H. Elliott, Santa Barbara, Calif.—In presenting this paper, Wills made a strong plea for cooperation between internist and surgeon in both the preoperative and the postoperative care of the patient. He pointed out that the internist is of great value in directing the administration of vitamins, in the direction of the treatment of patients with damaged livers, in the correct maintenance of water balance, and in the estimate of cardiac efficiency.

REPORT OF THE MEETING OF THE AMERICAN ORTHOPAEDIC ASSOCIATION, KANSAS CITY, MO., MAY 6-9, 1940

GUY CALDWELL, M.D., NEW ORLEANS, LA.

THE clinical demonstrations, papers, and discussions at the recent meeting of the American Orthopaedic Association covered many interesting subjects, varying from the feeding of oyster shells to hasten the healing of fractures to the effect of local implantation of sulfanilamide in joints and other tissues.

C. B. Francisco, Kansas City, administered 0.5 drachm of pulverized oyster shell (as prepared for chicken feed) three times daily to patients with recent and old fractures with delayed union and found that early and rapid callus formation followed.

Frank R. Treachenor, Kansas City, reported an interesting case of extradural spinal cyst which occurred in a boy 14 years of age who had a curvature of the spine with widening of the spinal canal at the junction of the dorsal and lumbar spines and fatigue and weakness of his legs. A laminectomy was performed two months after the onset of symptoms of paraplegia. Upon removal of the laminae there appeared a cyst which ruptured with the escape of clear fluid. The sac was carefully dissected away from the spinal cord and found to have a pedicle opposite the eleventh dorsal nerve root which appeared to be a herniation of the arachnoid through the dura. Following removal of the cyst, recovery was uneventful and the patient regained good use of his legs.

Ferdinand Helwig, Kansas City, discussed the relation of trauma to coronary artery disease and reported several cases of death from coronary disease which had occurred at short intervals following accidents. He had conducted an investigation with experimental work on rabbits by which it was shown that young rabbits withstood rather severe trauma in the region of the heart without dying or developing evidence of coronary disease as revealed by electrocardiographic tracings. Similar experiments conducted on old rabbits whose arteries had been previously rendered atheromatous by administration of cholesterol resulted in their death within fifteen minutes with electrocardiographic tracings indicating coronary occlusion and the lesions being verified by autopsy.

Rex Diveley, Kansas City, reported on complications encountered in the nailing of fresh fractures of the neck of the femur as shown in a survey of 100 cases two years after their operations. He was able to report the end results in 95 cases, 56 of which were treated in the General Hospital and 39 in private practice. He found the results differed considerably in the two groups. The mortality for the entire 95 cases was 11.5 per cent; it was only 2.5 per cent in the private cases as contrasted with 17.8 per cent in those at the General Hospital. Union had occurred in only 87 per cent of the entire series; excellent functional results were obtained in 60.5 per cent, good results in 20.2 per cent, and poor results in 13.3 per cent.

The poor results in those who obtained union were attributed to arthritis, degeneration of the head, and faulty relation of the head and neck. As an aid to the nailing procedure, a portable developing box was demonstrated. This box could be wheeled into the operating room and films developed in warm solution (72° F.), making it possible for the position and direction of the nail to be determined within two minutes.

Frank Dickson, Kansas City, presented the cases of a patient with infantile paralysis and curvature of the spine treated by the insertion of fascial transplants after the method of Lowman and a second patient with spinal deformity and weak-

ness associated with paralysis of the quadratus lumborum which was likewise entirely relieved by fascial transplant.

The value of fasciotomy of the tensor fascia femoris for relief of the stooped posture associated with spondylitis was well illustrated by one patient who was presented.

A motion picture was shown illustrating the correct technique for synovectomy of the knee and several patients upon whom the operation had been performed with most satisfactory improvement, including one patient with multiple atrophic joints.

S. Kleinberg, New York City, gave a paper on **The Obstetric Experiences of Women Paralyzed by Acute Anterior Poliomyelitis**. A large group of patients who had been paralyzed in childhood and had subsequently become pregnant were reviewed by x-ray studies of the pelvic inlet and passage. The films were taken with the patient in a semisitting position and the measurements determined by use of a calibrated grid. Of 101 patients so examined, asymmetrical pelves were found in 80 per cent and normal pelves in only 40 per cent. While flattening and asymmetry of the pelvis were almost universal in the women who had suffered from infantile paralysis previously, the deformities were not sufficient to interfere with normal delivery in the majority.

A second group of 13 cases was reviewed in which pregnancy was complicated with acute anterior poliomyelitis. Of the 13, 12 proceeded to normal delivery with normal children and a miscarriage occurred in 1. The incidence of cesarean section in a whole group was unduly high, probably because obstetricians were unduly afraid of complications. Further analysis, with reference to the average number of hours in labor and abnormal presentations which necessitated the use of forceps, indicated no wide variations from the average in similar groups of individuals not affected with infantile paralysis. In no case was a child infected with poliomyelitis even though born while the mother was acutely ill. Previous reconstructive operations for deformities following infantile paralysis did not interfere with delivery even when there had been such formidable operations as fusion of the hip or spine or such delicate procedures as fascial transplants to replace abdominal muscles.

George Wagoner, Philadelphia, presented a paper on **Chemistry of Normal and Arthritic Cartilage**. He had conducted a series of observations upon bovine articular cartilage with relation to age, sex, and breed of cattle, as a result of which he believes that the degenerative joint changes in cattle are largely the result of diminishing ability of the cell to consume oxygen as the animals grow older.

The Surgical Treatment of Degenerative Arthritis of the Knee Joint, G. E. Haggart, Boston.—The author summarized the results obtained in 20 selected patients whose ages averaged 56 years upon whom he had performed the operation of synovectomy five years to nineteen months prior to the review. All of these had been improved with respect to range of motion, stability of the joint, absence of swelling, partial or complete absence of pain, and better contour and texture of the bones as revealed by subsequent x-ray studies. Since 1935 Haggart has routinely excised the patella when doing the operation of synovectomy and of late has employed the split patella incision. He is careful to remove all synovial tissue from the anterior compartment, both semilunar cartilages, all marginal outgrowths of cartilage and to smooth off the areas of central erosion.

Arthur Steindler, Iowa City, presented a paper on **Treatment of Scoliosis by Combined Methods**. He discussed the groups of cases which may be expected to respond to corrective exercises and bracing and stated that most so-called idiopathic cases may be managed in this way. The curvatures associated with congenital anomalies of the spine and those following infantile paralysis in most instances require correction in plaster followed by fusion in the corrected position.

REPORT OF THE MEETING OF THE AMERICAN ORTHOPAEDIC ASSOCIATION, KANSAS CITY, MO., MAY 6-9, 1940

GUY CALDWELL, M.D., NEW ORLEANS, LA.

THE clinical demonstrations, papers, and discussions at the recent meeting of the American Orthopaedic Association covered many interesting subjects, varying from the feeding of oyster shells to hasten the healing of fractures to the effect of local implantation of sulfanilamide in joints and other tissues.

C. B. Francisco, Kansas City, administered 0.5 drachm of pulverized oyster shell (as prepared for chicken feed) three times daily to patients with recent and old fractures with delayed union and found that early and rapid callus formation followed.

Frank R. Treachenor, Kansas City, reported an interesting case of extradural spinal cyst which occurred in a boy 14 years of age who had a curvature of the spine with widening of the spinal canal at the junction of the dorsal and lumbar spines and fatigue and weakness of his legs. A laminectomy was performed two months after the onset of symptoms of paraplegia. Upon removal of the laminae there appeared a cyst which ruptured with the escape of clear fluid. The sac was carefully dissected away from the spinal cord and found to have a pedicle opposite the eleventh dorsal nerve root which appeared to be a herniation of the arachnoid through the dura. Following removal of the cyst, recovery was uneventful and the patient regained good use of his legs.

Ferdinand Helwig, Kansas City, discussed the relation of trauma to coronary artery disease and reported several cases of death from coronary disease which had occurred at short intervals following accidents. He had conducted an investigation with experimental work on rabbits by which it was shown that young rabbits withstood rather severe trauma in the region of the heart without dying or developing evidence of coronary disease as revealed by electrocardiographic tracings. Similar experiments conducted on old rabbits whose arteries had been previously rendered atheromatous by administration of cholesterol resulted in their death within fifteen minutes with electrocardiographic tracings indicating coronary occlusion and the lesions being verified by autopsy.

Rex Diveley, Kansas City, reported on complications encountered in the nailing of fresh fractures of the neck of the femur as shown in a survey of 100 cases two years after their operations. He was able to report the end results in 95 cases, 56 of which were treated in the General Hospital and 39 in private practice. He found the results differed considerably in the two groups. The mortality for the entire 95 cases was 11.5 per cent; it was only 2.5 per cent in the private cases as contrasted with 17.8 per cent in those at the General Hospital. Union had occurred in only 57 per cent of the entire series; excellent functional results were obtained in 60.5 per cent, good results in 20.2 per cent, and poor results in 13.3 per cent.

The poor results in those who obtained union were attributed to arthritis, degeneration of the head, and faulty relation of the head and neck. As an aid to the nailing procedure, a portable developing box was demonstrated. This box could be wheeled into the operating room and films developed in warm solution (72° F.), making it possible for the position and direction of the nail to be determined within two minutes.

Frank Dickson, Kansas City, presented the cases of a patient with infantile paralysis and curvature of the spine treated by the insertion of fascial transplants after the method of Lowman and a second patient with spinal deformity and weak-

was performed after the fracture had occurred, the better the result. In 25 cases there had been 1 nonunion and 2 complaints of stiffness and pain; all had at least 75° of flexion.

Beveridge Moore of Chicago presented his thesis on the "Orthopedic Relationships of Neurofibromatosis." He stated that the skeletal changes associated with neurofibromatosis consist of scoliosis, growth changes, bone changes and the condition called congenital pseudarthrosis. He reviewed four cases of localized hypertrophy, e.g., enlargement of the second and third fingers, and overgrowth of the foot and leg on one side, associated with the typical skin lesions, and familial history of neurofibromatosis. In all cases he found a neurofibroma in the nerve supplying the affected parts.

He also reported three cases of congenital pseudarthrosis of the tibia associated with Von Recklinghausen's disease, in all of which typical neurofibromata were found in the posterior tibial nerves. Microscopic sections of the nerve tumors revealed endarteritis of the vessels.

A symposium was then conducted on The Incidence, Significance, and Treatment of Sciatic Pain in Low Back Cases. Theodore A. Willis, Cleveland, discussed the Anatomical Variations as Well as Roentgenological Appearance of Low Back Pain in Relation to this Subject. He stated that bilateral enlargement of the transverse processes of the fifth lumbar vertebra probably is not a cause for low back pain and sciatica, but believes that asymmetrical fusion of a transverse process or variations in the position and angles of the lumbosacral facets and narrowing of the intervertebral disk, congenital or acquired, may produce pressure on the nerve roots and bring about pain. The soft part changes and poor anchorage for supporting ligaments associated with spina bifida he believes to be sufficient cause for low back pain and sciatic radiation. Lateral defects in the neural arches resulting in spondylolisthesis he considers the probable result of a fracture of the lamina in early infancy and constituting reason for low back pain.

W. McK. Craig, Rochester, Minn., discussed the Neuro-Anatomy and Physiology—Significance of Sciatica, reviewing the embryological development and distribution of the lower spinal nerves. He then discussed many of the symptoms by which central cord tumors might be differentiated from those making pressure on the nerve roots or peripheral portions of the nerves.

John G. Kuhns, Boston, reviewed Conservative Treatment, having reviewed 1,000 cases of low back pain. Of these he considered 579 to have been of muscular origin and 325 associated with strain of the ligaments. The symptom of sciatic pain, although not constant, was present in 449 cases; pain was referred to the regions supplied by the common peroneal in 410 cases, and in 80 per cent of all cases it appeared that the symptom of sciatic pain was of reflex origin and associated only with strains or tears of the supporting ligaments in the lumbosacral area. The diseases and anomalies found to be associated were as follows: hypertrophic arthritis, 96; atrophic arthritis, 70; transverse lumbosacral facets, 64; spina bifida, 50; and defective facets in a smaller number.

The treatment of the great majority of cases, therefore, should be conservative.

For the group of muscular and ligamentous strains and tears the early treatment should consist of rest with the injured parts in a relaxed position; patients with low back pain should be kept supine with the back flattened by flexing the hips or on their faces with a pillow under the abdomen. Physiotherapeutic treatments can be administered in the latter position. As soon as the severe spasm of the muscles relaxes, the patient can begin gradually to sit up with the aid of good spinal support. While the period of recumbency necessarily varies with the severity of the injury, in Kuhns' cases it averaged ten days.

A Study of Over 100 Paralytic Scoliotics was presented by Paul C. Colonna and Frederick Von Saal, Oklahoma City. In a follow-up study of patients seen in their hospital over a period of twenty years, it was found that 30 per cent of 500 cases of infantile paralysis had developed spinal curves and that 62 per cent of all the cases of scoliosis under treatment had resulted from infantile paralysis. The majority of cases of scoliosis developed in those whose trunk muscles had been affected by the paralysis and the records revealed that very few of these had been given recumbent treatment in the early months of their illness and that back supports had not been employed in more than 20 per cent of the cases. They believe, therefore, that in every child who has indications of trunk involvement in the early stages of infantile paralysis the following measures should be used to prevent the development of scoliosis: (1) recumbency for six months and (2) early supervised muscle training.

M. N. Smith-Petersen, Boston, discussed his operation of Acetabuloplasty: **An Analysis of Results.** It is his opinion that, since the development of the improved technique for arthroplasty of the hip, there is a very limited field for the operation of acetabuloplasty. Nevertheless, the approach to the hip joint which was developed and first described in connection with the operation of acetabuloplasty has made it possible to do arthroplasties with greater ease and with better results. He reported that 53 patients on whom he had performed acetabuloplasties were traced; the mortality was 4 per cent; the operation had been satisfactory to the surgeon and the patients in 50 per cent, satisfactory to the patient only in 19 per cent, and unsatisfactory to both in 31 per cent. It was found that 50 to 75 per cent of the patients who had *malum coxae senilis* were relieved.

Henry L. Jaffe, New York City, presented a paper on **Osteoid Osteoma. Further Experience With This Peculiar Lesion of the Bone.** He described this as a benign tumor which begins in the spongiosa or cortex near the periosteum, a new growth of small size that occurs in adolescents and young adults between the ages of 16 and 24 years. The symptoms consist of localized pain in the bone with none of the signs of inflammation and x-ray examination reveals an opaque nidus surrounded by a circular area of rarefaction and these in turn by pronounced osteosclerosis. The lesions have been thought to be of inflammatory origin and frequently have been called osteomyelitis. He reported 9 cases which had occurred in phalanges, neck of the astragalus, scaphoid, head of the fibula, os calcis, ulna, and the femur.

Frederick C. Kidner, Detroit, discussed **Subtrochanteric Osteotomies, Indications for Special Types.** In his experience the intertrochanteric osteotomy described by McMurray had not been uniformly successful for nonunion of the neck of the femur. He had found the curved subtrochanteric osteotomy useful in cases of deformity of the head of the femur occurring in young people. He then discussed the use of subtrochanteric osteotomy in a group of 5 cases of tuberculosis of the hip which had not progressed satisfactorily by the use of routine measures of fixation and plaster.

Randolph S. Reich, Cleveland, reported on the use of **Bifurcation Osteotomy for the Treatment of Ununited Fractures of the Femoral Neck.** He had performed this operation on 26 patients with nonunion following fractures of the hip and failed to get union in only 2. In all cases the operation was done after six weeks or longer and the femoral heads were viable. He believes the operation is contraindicated on patients with osteoarthritis or on those who are poor surgical risks. He follows the technique described by McMurray and is careful to divide the femur completely with the osteotome to avoid any projecting spicules which may occur when the bone is fractured. In his experience the earlier the operation

With reference to the residual low back symptoms, 60 per cent had normal backs; 32 per cent had slight back pain; and 8 per cent had severe disabling pain. It was Barr's opinion that, when instability of the spine is suspected or demonstrated, fusion should be done at the time of the laminectomy.

W. B. MacCracken, New York City, presented a paper in conjunction with Benjamin P. Farrell, New York City, on **Lumbosacral Lesions With the Exception of Spondylolisthesis**. In answer to the question, "Is laminectomy and removal of a ruptured disk the only treatment?" the records of the New York Orthopedic Hospital had been reviewed from 1914 up to the present time. Thirty-three patients have been operated upon since 1937 in that institution by performance of laminectomy followed by fusion of the spine. The most common findings in these cases were arachnoid adhesions associated with a small disk protrusion.

The records of 175 patients who had fusion operations for sciatic pain were reviewed and 46 of these were found to have recorded some or all of the signs suggesting a ruptured intervertebral disk. Of these 46 patients, 27 were recalled and their results reviewed. The percentage of good results in this group was practically the same as in the group which had been operated upon since 1937 by performance of laminectomy and fusion; namely, about 83 per cent had good or perfect results. Five cases were found upon whom laminectomy had been performed following old fusion operations. Only 1 of these was found to have ruptured disk and the other 4 were not relieved. Their conclusions were that an absolute diagnosis of rupture of the intervertebral disk is difficult at best and that the operation of spinal fusion in most cases of low back pain with sciatica offers as good a chance of success as laminectomy.

M. N. Smith-Petersen, Boston, discussed **Sacroiliac Conditions** and explained that sciatic pain may accompany disease and trauma of the sacroiliac joint and when it does so the clinical picture may be quite similar to that produced by rupture of the intervertebral disk. He made a plea for more accurate interpretation of symptoms of sciatic pain and emphasized the importance of recording accurately the angles at which straight leg raising aggravates sciatic pain. He also stressed the importance of differentiating hyperesthesia from actual tenderness. If sciatic pain is present before the leg is raised to an angle of 30°, no part of the spine having been moved, the pain must result from hyperesthesia alone and suggests the presence of an intraspinal lesion. When sciatic pain occurs as the leg passes between the angles 30 and 60°, the sacroiliac ligaments are then under tension, and the lesion is probably in or about the sacroiliac joint. When the leg has been raised to 70°, or higher, motion takes place in the lumbar spine and the lesion should be located in those joints.

The results obtained by sacroiliac fusion in 100 cases were complete relief in 88, partial relief in 8, and unsuccessful results in 4.

Henry W. Meyerding, Rochester, Minn., discussed **Incidence Significance and Treatment of Low Backache and Sciatic Pain Associated With Spondylolisthesis**. He explained that the outstanding symptom of spondylolisthesis is low back pain, not sciatica. He had found, however, that protrusion of a ruptured disk may coexist. Among 745 cases of spondylolisthesis there were 80 patients who complained of sciatica. These symptoms occurred more frequently in Grades 1 and 2 of spondylolisthesis than in Grade 3. It is evident that forward slipping of the body of one vertebra upon another enlarges the intervertebral foramen and therefore gives little cause for sciatic pain. In the few patients who were found to have a coexisting protrusion of the intervertebral disk, laminectomy with removal of the protruding mass preceded the spinal fusion which should always be done for spondylolisthesis.

Frank Ober, Boston, advocated the performance of fasciotomy of the tensor fasciae femoris when there was demonstrable contracture of this fascia associated

The spinal support employed in the convalescent treatment should be one that has a firm grip on the pelvis, should extend well above and below the lumbosacral articulation, and should retain the lower back in good functional position (i.e., midway between flexion and extension). Further treatment should consist of general measures to improve health and reduction of weight in the obese cases. The spinal support should be discarded gradually rather than abruptly. The total period of treatment averaged forty-eight days, with the following results: cured, 6.3 per cent (the patients returned to their work and complained of no symptoms for at least six months afterward); unimproved, 6.2 per cent; improved, 87.5 per cent (approximately). He observed that many of those who were only improved had arthritis and spinal anomalies. He suggested that the prognosis should depend upon whether the lesion was the result of injury to the muscles and ligaments, a lesion of the vertebrae or their articulations, an intraspinal lesion (tumor or protruded disk), or a visceral lesion in the pelvic organs.

Joseph S. Barr, Boston, reviewed the subject of *Intervertebral Disk*, reporting the cases operated upon by W. J. Mixer. There were 99 cases, of which 2 occurred between the third and fourth lumbar vertebrae, 57 between the fourth and fifth, and 40 between the fifth lumbar and the sacrum. Many were associated with thickening of the ligamentum flavum.

The etiology appeared to be a rupture of the annulus fibrosus from sudden pressure in some cases and development of a fissure from wear and tear or gradual extension. The average age of all patients was 37 years but 80 per cent occurred between the years of 30 and 50. Eighty per cent of all cases gave a history of injury, such as lifting, having a fall, or making a sudden twisting movement. Backache preceded the sciatic symptoms in 30 to 40 per cent of the cases; recurrences and remissions had occurred in 40 per cent and the sciatica had been continuous from the onset in 60 per cent. The symptoms were unilateral in 80 per cent and bilateral in 20 per cent of the cases.

Examination of the patients revealed sciatic scoliosis present in 60 per cent and a reversed lumbar curve in 90 per cent. Straight leg raising was restricted in 95 per cent of the patients' affected sides and in 30 to 50 per cent of the opposite sides. Local tenderness was present over the spinous process of the fifth lumbar vertebra in 50 per cent. Sneezing caused sciatic pain in 40 per cent; muscular atrophy was present in 40 per cent and a diminished ankle jerk in 70 per cent. Sensory changes occurred most frequently on the lateral aspect of the foot and were present in 35 per cent of the cases; motor weakness was present in 15 per cent and loss of sphincteric control in 5 per cent. Narrowing of the intervertebral space was present in 50 per cent of those having ruptured disks and appeared to be quite significant when it occurred between the fourth and fifth lumbar vertebrae; however, at the lumbosacral junction the narrowing was less significant. No single symptom or sign has been found which is definitely diagnostic of this lesion. Injection of air into the spinal canal followed by roentgenographic examination gave positive finding in only 50 per cent of the cases, while the lipiodol studies were positive in practically all cases.

Operation is always reserved for those who have not responded to conservative treatment. Patients are advised to perform no heavy labor for at least six months after the operation and to resume active exercises very gradually. It was found that some of those with positive lipiodol studies who declined operation obtained relief by having a plaster jacket applied with the spine slightly flexed. Ninety-four patients had been operated upon for more than one year and in this group 77 per cent had complete relief of sciatic pain; 18 per cent had only minor complaints, and 5 per cent were failures, 2 cases of which were proved to have developed recurrence of the herniated disk. In 35 per cent of the cases spinal fusion had been done at the time of operation and in 65 per cent it was omitted. The results were slightly better in the group which had spinal fusion performed.

changes are well under way. The earliest signs consist of limited movements of the hip and thickening of the capsule. Pathologically the process is one of aseptic necrosis of the neck and head of the femur beginning primarily in the metaphysis and progressing to the head. Healing likewise appears first in the metaphysis and subsequently in the head. Deformities of the head and neck of the femur are the direct result of weight-bearing and muscular pulls and such deformity as occurs in the acetabulum is secondary to that of the head of the femur. Prolonged rest in bed with extension attached to the leg will prevent malformation of the head. Complete relief from weight-bearing is essential until the regenerative phase is almost complete. Partial or intermittent weight-bearing and various medical and operative treatments that have been advocated from time to time were not successful.

Wallace H. Cole, St. Paul, Minn., discussed the treatment of Clawfoot. This deformity may result from several different causes, all of which bring about weakness of certain groups of muscles in the foot and leg. The milder earlier cases have responded to manipulation for stretching the plantar structures, the use of metatarsal supports and night splints. Other cases require, in addition, plantar fasciotomy and wrenching of the foot or a stripping of the os calcis followed by the application of plaster for three weeks and physiotherapy thereafter. When there is some varus deformity, he has found it wise to transplant the toe extensors into the cuneiform bone and at the same time perform a fusion of the interphalangeal joint of the great toe. The aftertreatment consists of immobilization in plaster for six weeks followed by weight-bearing in a shoe with an anterior heel.

Cases with marked bony deformity cannot be corrected by the foregoing procedures but require removal of an anterior tarsal wedge of bone, distal to the scaphoid. He does not at the same time perform a subastragalar arthrodesis.

Albert Key, St. Louis, discussed *The Effect of Local Implantation of Sulfanilamide in Joints and Other Tissues*. By animal experimentation, the local implantation of sulfanilamide crystals which have been sterilized in the autoclave produces no unfavorable tissue reaction, does not retard healing. He prefers to use a citrated solution of sulfanilamide in the joints themselves or to inject the solution neoprontosil. His experiments did not include the introduction of infectious material into the tissues and joints followed by implantation of sulfanilamide. The effect of the chemical in concentrated solution on cultures of *B. welchii*, streptococci and staphylococci in vitro demonstrated it to be effective in varying degrees, even when acting in a medium favorable to the propagation of the organisms; that is, a medium which included peptones.

THE FIFTY-SECOND ANNUAL MEETING OF THE AMERICAN
ASSOCIATION OF GENITOURINARY SURGEONS,
SKYTOP, PA., JUNE 20-22, 1940

C. D. CREEVY, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

ON JUNE 20, the following papers were given:

A. L. Dean and W. L. McCarthy, New York City, described a case of persistent, profuse left renal hematuria in a child who had hemangiomas of the left leg, nose, and lip, and an area of calcification in the brain. On removal the kidney contained a benign, centrally located hemangioma.

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with sciatica. He has performed this operation on 86 patients who had sciatic pain, in many of whom the pain was bilateral and relieved only by operation on both sides. The results obtained were excellent in 38 cases, marked improvement in 30, slight improvement in 5, no improvement in 5.

Clarence H. Heyman, Cleveland, reported that the operation of stripping the muscular and fascial attachments from the posterior aspect of the sacroiliac joint and ilium is indicated for superficial lesions of a chronic type as indicated by localized tenderness over the posterior-superior spine of the ilium near the periosteal attachments of the muscles, in which injections of novocain give temporary relief. The operation of subperiosteal stripping serves to relieve the tension and has been performed by him in 29 cases, of which 26 obtained relief.

Carl E. Badgley, Ann Arbor Mich., reviewed *The Relation of Facets and Ligaments to Low Back Pain and Sciatica* and stated that asymmetrical facets appear to be a factor in 52 per cent of the cases.

Conservative Treatment of Low Back Pain and Sciatica was discussed by George E. Bennett, Baltimore. He emphasized conservative treatment for the great majority of these cases because they are the result of strains and falls, poor posture, and arthritis. Those resulting from strains and sprains respond well to rest in bed, physiotherapy, the use of spinal support, and graduated exercises. Those secondary to falls he believes to be associated with slight displacements and finds that most of them respond to manipulation of the spine by hyperflexion of the legs with or without anesthesia. Postural backaches respond to rest and corrective exercises. Many of the chronic backaches reveal deviations of the spine which follow an old injury and are probably a result of the formation of adhesions. He finds that many of these respond to manipulation followed by suitable measures of physiotherapy.

Rex Diveley, Kansas City, reported that he had reviewed the fusion operations done in their clinic in 70 cases with the following findings: fusion of the sacroiliac joint, 3 cases; fusion of the sacroiliac and lumbosacral joints, 4 cases; and lumbosacral fusion, 63. Ninety per cent were relieved entirely; 2.8 per cent had only partial relief; 7.2 per cent obtained no relief and further investigation of the later group revealed the presence of a ruptured disk in all of them.

Philip D. Wilson, New York City, presented a report on the *Two-Stage Side Transplantation of the Fibula for Complicated Pseudarthrosis of the Tibia*. The operation is done in two stages at intervals of four to six weeks, the fibula being divided at the upper and lower extremities and inserted into a prepared bed in the lateral aspect of the ununited tibia. The operation has been successful in cases of nonunion following old compound fractures with loss of substance even though repeated massive grafts had previously been tried and failed. It was noteworthy that following union of the fibula to the shaft of the tibia above and below the site of fracture, the fracture itself subsequently united.

The larger series of cases consisted of congenital pseudarthroses in which failures had occurred previously with various types of bone grafts. In this group union of the tibia had occurred following fusion of both ends of the fibula with the tibia.

A. Bruce Gill, Philadelphia, discussed *Legg-Perthes' Disease With Particular Reference to Its Earliest X-Ray Manifestations and Its Cyclical Course*. He stated that there is a phase of degeneration lasting about one to one and one-half years followed by regenerative phases for two to three years. It has been definitely shown that relief from weight-bearing shortens the duration of both phases. This trouble occurs in boys in 85 per cent of cases and only between the ages of 3 and 11 years. At the time symptoms are first manifested the pathologic

2 still had pyuria for from three to six years after operation, thus reinforcing the growing belief that plastic procedures should be more widely employed in this condition.

The following papers were read on June 21:

H. G. Hamer and H. O. Mertz, Indianapolis, reported the findings at autopsy in a case of nonparasitic chyluria of long standing. It proved to be due to obliteration of the thoracic duct by a surrounding tumor, apparently inflammatory, with stricture of the duct and occlusion of the subclavian vein by an old thrombophlebitis. Chyle reached the urine from ruptured, dilated lymphatics in the wall of the bladder.

C. L. Deming and J. F. Sadusk, New Haven, Conn., discussed three cases of anuria due to sulfapyridine crystals in the renal pelvises and ureters. Two recovered after lavage of the pelvis through indwelling ureteral catheters with warm (106° F.) sterile water. One died of cerebral edema.

G. G. Smith and W. F. Leadbetter, Boston, found that, since neopax and diodrast are eliminated through the renal tubules, the excretion of phthalein is a better indication of the probability of success or failure of an excretory urogram than is the level of nitrogen in the blood. Occasionally one may get readable urograms with a nonprotein-nitrogen as high as 50, and with inability to concentrate the urine to a level above 1.003 to 1.006.

A. H. Paine, Rochester, N. Y., reviewed the diagnostic criteria of tumors of the ureter; chief among these are bloody spurts from the ureteral orifice while clear urine is obtainable from the renal pelvis and a filling defect in the urogram. He reported a papillary carcinoma of the ureter in a man 60 years of age.

A. R. Stevens, New York City, has found in the literature that at least 40 patients have lived 10 to 30 years after ureteroenterostomy, 11 of them for more than 20 years. Two of his personal cases are living 11 and 29 years; he has seen one alive 43½ years after operation by Fowler. This is heartening information.

E. L. Keyes, New York City, advocates cutaneous ureterostomy in certain cases of intractable vesical tuberculosis. In those whose only kidney is not tuberculous, indwelling catheters may be discarded after the skin and ureter have united, and a colostomy cup employed. If the kidney is tuberculous, an indwelling catheter is required. Three patients have done well without catheters for from three to nineteen years.

P. G. Smith, Cincinnati, prefers temporary ureterostomy or nephrostomy as an emergency measure when ureteral injury is not discovered until after operation. He reported two cases in which the terminal ureter had been irreparably damaged on one side and was too short for reimplantation into the bladder, and in which anastomosis was not feasible. He cut off the ureter above the site of injury and anastomosed it to the sound ureter retroperitoneally with good results.

H. O. Mertz, Indianapolis, described a case in which hematuria was due to chloroma of the bladder and kidneys in a 12-year-old child. The blood picture was that of myeloid leucemia; at necropsy there were greenish tumors of the kidneys, bladder, spinal cord, and lymph nodes.

W. E. Lower, Cleveland, described a method of biologic assay of the hitherto elusive hormone, inhibin, said to be formed by the germinal epithelium of the testes, and to prevent that overactivity of the hypophysis which is thought by some to cause hypertrophy of the prostate. The daily injection of potent extracts will suppress estrus in the rat; injection of extracts of liver prepared in the same way fails to do so.

Leon Herman and Max Strumia, Philadelphia, discussed hemorrhagic cysts of the kidney and distinguished them from serous cysts with secondary hemorrhage.

H. G. Bugbee, New York City, advocated operation in those cases in which the history, physical examination, and pyelogram, repeated at intervals, are suggestive but not characteristic of renal tumor.

W. N. Wishard, Jr., Indianapolis, reported an example of inoperable chorioepithelioma which apparently originated in the retroperitoneal tissues and simulated a renal neoplasm. The testes were normal.

Leon Howard, Denver, showed a moving picture of a malignant neoplasm of the adrenal cortex in a 26-year-old female with hirsuties, a masculine voice, hypertrophy of the clitoris, and amenorrhea. It was demonstrated by radiography after the perirenal insufflation of air, removed surgically, and irradiated. The patient has been well for some time and has lost her masculine characteristics. The ultimate prognosis, however, is poor because of the nature of the tumor.

In the discussion G. F. Cahill, New York City, stated that production of cortical hormone by a tumor may lead to atrophy of the opposite adrenal, so that the postoperative reaction is likely to be severe even though a proper pre- and post-operative regime is employed. If no reaction occurs, it suggests the possibility of metastases which supply hormone.

G. C. Prather and Weston Sewall, Boston, investigated pyelonephritis as a possible etiologic factor in toxemia. Ten per cent of pregnant women exhibit evidences of toxemia; 1 to 2 per cent of pregnant women develop pyelonephritis of some degree; 12.5 per cent of the patients who have had pyelonephritis in a previous pregnancy develop toxemia in a subsequent one. The authors conclude that pyelonephritis probably has no causal relation to toxemia.

J. B. Wear, Madison, Wis., in a study of 109 cases did not feel that he could demonstrate that the retention of urine in prostatism caused elevation of the blood pressure; urograms failed to demonstrate a higher incidence of hydro-nephrosis in patients with hypertension than in those with normal blood pressure.

W. F. Braasch, Rochester, Minn., found 47 instances of hypertension in 180 cases of chronic pyelonephritis. It was commoner in those with marked pyelographic changes and in those with impaired renal function. Twenty-six per cent of patients with pyelonephritis had hypertension as compared to 20 per cent of controls in the same age group. Braasch feels that pyelonephritis may serve as an irritant and bring out a latent hypertension; he does not believe that it can produce hypertension in the otherwise normal person.

In the discussion Alexander Randall, Philadelphia, suggested that hypertension may occur in prostatitis with intrarenal pelves.

G. W. Fish, New York City, discussed a patient who was known to have a normal blood pressure after carrying 1,000 c.c. of residual urine for two years. His pelves were intrarenal and undilated.

F. H. Colby, Boston, advocated sanatorium care in renal tuberculous; he is impressed with its value both before and after operation, although it will not produce cures unaided. He has found guinea pig inoculation more accurate than culture as a diagnostic measure; albuminuria in a tuberculous patient strongly suggests involvement of the kidney.

T. P. Shupe, Cleveland, treats noncalculous obstruction at the ureteropelvic juncture by a modified Fenger plastic (longitudinal incision, transverse closure) performed from within the pelvis. Of 9 patients 3 were symptom free, although

of Chevassu and Hinman). At present about 30 per cent of the cases are being controlled for five years or more by intensive irradiation (including the abdomen and chest) followed by orchidectomy and later by more irradiation.

Alexander Randall and G. W. Chamberlin, Philadelphia, treat testicular tumors by irradiation, in sequence, of the supraclavicular area, the chest, the abdomen, and last, the testis. Orchidectomy is done four weeks later. Eleven of 12 patients so treated are living two or more years. The method was evolved after a patient with a palpable abdominal metastasis was found to be well some years later; 3 of 8 such patients are well for three years or more.

G. F. Cahill, New York City, reported that he had done the radical operation in 18 of 55 testicular tumors between 1929 and 1939. Fourteen are well for one to eleven years, 4 of these for more than nine years.

THE THIRTY-SEVENTH ANNUAL MEETING OF THE AMERICAN UROLOGICAL ASSOCIATION, BUFFALO, N. Y., JUNE 24-27, 1940

C. D. CREEVY, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

THE meeting was opened on June 24 with the following papers:

C. A. W. Uhle, Philadelphia, has seen four cases of aneurysm of the abdominal aorta mimicking renal disease. In one the findings suggested perinephritic abscess; in the others pain simulating renal colic was produced. The dangers of operating under an incorrect diagnosis were emphasized.

H. H. Howard, H. I. Suby, and James Harberson, Boston, reported a successful nephrectomy for aneurysm of the renal artery. The condition is found once in 7,500 necropsies and may result from trauma, severe infection, arteriosclerosis, and syphilis. Preoperative diagnosis usually depends upon demonstration of a ringlike density medial to the renal hilus in the x-ray.

C. M. McKenna and J. H. Kiefer, Chicago, advocated preservation of useful renal tissue by the employment of conservative operations, such as plastics upon the ureteropelvic junction. The importance of nephrostomy was emphasized.

G. C. Prather, Boston, operated successfully upon three cases of diverticulum of the calyx renalis, also called pyelogenic or urinary cyst, or hydrocalicosis. One, being peripheral, was excised and two, being central, were evacuated and drained by nephrostomy.

O. S. Lowsley and J. H. Menning, New York City, ruptured the kidney experimentally and found that more useful tissue survived if the clots were evacuated, hopelessly damaged tissue removed, and the bleeding controlled by ribbon catgut, than if nonsurgical treatment was employed. They advocate operation for rupture of the kidney if hematuria persists after twenty-four hours.

In discussion W. J. Engel, Cleveland, believes so-called calyceal diverticulum to be a calyx dilated as the result of stricture of its neck. He objects to Lowsley's indications for operation upon ruptured kidney and has operated in but 2 of 17 cases.

E. M. Watson and C. C. Herger, Buffalo, N. Y., described the treatment of 512 cases of carcinoma of the bladder at the New York State Institute for the Study

On the final day of the meeting, June 22, the following papers were presented:

A. I. Dodson, Richmond, Va., was able, in two instances of destruction of a considerable portion of the bulbous urethra, to repair the defect by excising the damaged tissues, bridging the roof of the defect with a mucosal flap from the adjoining intact urethra and covering the defect with a fascial flap from the scrotum. In the second case a large defect in the perineal skin was replaced by a flap of scrotal skin.

D. M. Davis, Philadelphia, has been dissatisfied with Thiersch's urethroplasty for hypospadias because the new external meatus is behind the glans. He has, therefore, after a preliminary Duplay plastic to straighten the penis, fashioned a tubular flap with skin inside from the skin of the dorsum of the penis. Its pedicle is attached to the base of the penis, its distal end cut free. The penis is bent dorsally and the glans and ventral skin behind it are perforated by a trocar. The tube is drawn through the perforation and its end sutured to the edges of the perforation in the ventral skin. After healing, it is cut off at its entrance into the glans. The defect between the posterior end of the new segment and the anterior end of the old urethra is closed at a third session by the method of Thiersch.

R. M. Nesbit, Ann Arbor, Mich., described a new method of straightening the hypospadiac penis. The foreskin is completely circumscribed behind the corona, dissected free back to the external meatus, and pulled up like a sleeve. The fibrous rudiment of the corpus spongiosum is completely excised so that the penis is straight. A transverse buttonhole is then made in the dorsum of the foreskin, and the glans brought through it and sutured. Thus redundant skin from the dorsum is transferred to the ventral surface of the penis. The defect left on the ventrum is sutured transversely. After healing there is a transverse scar on the ventral surface and an excess of redundant, mobile skin which enormously facilitates later urethroplasty without tension.

G. R. Livermore, Memphis, Tenn., has found that persistent symptoms after transurethral resection are due in the main to incomplete operation leaving tags and nodules which may cause straining, persistent infection, and bleeding. Resection of the abnormal tissue is required.

R. M. Nesbit and Edwin Davis, Omaha, Neb., each sent identical questionnaires to 100 consecutive patients operated upon for benign hypertrophy of the prostate at least one year before. Although all of Nesbit's patients were treated by transurethral resection and all of Davis' by perineal prostatectomy, results were almost identical except that there were two cases of partial and one of complete incontinence after perineal prostatectomy, while all those resected reported normal control. Postoperative hospitalization was nine days shorter after resection.

M. L. Boyd, Atlanta, Ga., discussed the formation of renal calculi in bed-ridden patients. The stones are usually composed of phosphates. Factors in their formation are: stagnation in dependent calices, concentration of the urine due to low intake of fluids, dietary deficiencies leading to alkaline urine, infection with urea splitters, and increased excretion of calcium due to disease of bone. Measures to prevent their formation include: mobilization of the patient, forced fluids, adequate acid ash diet, and vigorous treatment of infection.

E. S. Barringer, New York City, reviewed the autopsy findings in 37 cases of teratoma testis and concluded that: the Aschheim-Zondek test, properly done, is of prognostic value; the tumors are radiosensitive; aortic nodes are often involved before the iliacs; the left supraclavicular nodes are often involved; and crossed metastasis is common (which has led him to discard the radical operation

A. M. Grance, Geneva, N. Y., reported a bizarre example of the insertion of many needles into each testis by a patient with a mental aberration.

G. H. Ewell, Madison, Wis., C. R. Marquardt, and J. C. Sargent, Milwaukee, have treated 79 hydroceles in 71 patients by aspiration of the fluid and injection of quinine and urea hydrochloride. After one month to seven years 95.3 per cent were cured, a record not exceeded by open operation.

H. H. Young exhibited a colored motion picture of a plastic operation for the correction of a deformity of the penis following circumcision in which the glans and shaft were buried in the scrotum by the formation and contraction of scar tissue. The penis was freed, straightened, and covered with skin, and a displaced testis was brought into the scrotum.

John Scudder, New York City, summarized his work upon surgical shock which is based upon the experimental observation that the serum potassium rises remarkably just before death from hemorrhage and that this change affects the heart adversely. He described rapid methods for determining the sodium-potassium ratio and protein content of the plasma and discussed the selection of proper treatment based upon the results of these measurements.

On June 26 the following papers were presented:

G. J. Thompson, Rochester, Minn., concluded, from studying a large group of cases of leucoplakia of the bladder, that it is not a precancerous lesion.

A. I. Folsom, H. A. O'Brien, and G. T. Caldwell, Dallas, Tex., have treated interstitial cystitis (Hunner ulcer) by excising all of the bladder except the trigone and internal meatus, and a very small cuff of tissue around them. This method is based upon old experimental observations of the ability of the dog's bladder to regenerate after subtotal resection. Apparently the same phenomenon occurs in the human being with interstitial cystitis if severe infection is absent.

J. C. Kimbrough, Washington, D. C., found vesical diverticula in 8 per cent of obstructive lesions at the outlet of the bladder. He prefers extravesical diverticulectomy in those requiring surgical treatment.

R. E. Van Duzen, I. C. Winter, and Donald Slaughter, Dallas, Tex., observed the effect of trasentin upon the bladder of the unanesthetized dog. Forty-five minutes after administration the capacity of the bladder was 150 per cent of normal. Morphine ordinarily increases irritability and diminishes capacity. Trasentin counteracts the effect of morphine.

Erwin Neter, Buffalo, N. Y., described a series of experiments with bacteriostasis in vitro by sulfanilamide and related compounds upon various strains of enterococci. All were susceptible, and the effects of sulfanilamide, sulfapyridine, and sulfathiazol were increased by heat and by increasing the concentration of sodium chloride in the medium.

Grayson Carroll, Louis Kappel, and Bransford Lewis, St. Louis, discussed the effects of sulfathiazol and sulfamethylthiazol upon staphylococcal infections, in which sulfanilamide and sulfapyridine have been disappointing. Results have been encouraging in staphylococcal infections of the genitals, perinephrium, wounds, and in septicemia.

R. L. McKiernan, Brunswick, N. J., summarized five months' clinical experience with sulfathiazol. He found it especially effective in infections with the staphylococcus and gonococcus.

of Malignant Disease. X-ray alone is not satisfactory because, to deliver an adequate dose to the bladder, surrounding structures must be injured. Implantation of radon and electrocoagulation are most useful, being applied cystoscopically in small tumors and through a suprapubic incision in large ones.

F. H. Colby, Boston, described experiences with a million volt x-ray apparatus. It was possible to secure a greater depth dose with less injury to surrounding structures and less systemic reaction than with machines of lower potential. Anaplastic epithelial tumors were most and papillomas least sensitive. No Grade 1 tumors disappeared with irradiation, but 30, 50, and 66 per cent of tumors of Grades 2, 3, and 4 disappeared. Recurrences were common; it is too early to speak of end results.

W. C. Stirling and J. E. Ash, Washington, D. C., described and differentiated the common but rather obscure lesions of the mucosa of the renal pelvis, ureter, and bladder known as pyelitis, ureteritis, and cystitis cystica, follicularis, glandularis, and granulosa. They are thought to arise from extension of nests of mucosal cells into the submucosa in response to chronic irritation, usually infection. These nests, while appearing to become pinched off, are actually continuous with the lining epithelium. The center of the nest may break down and fill with fluid; cells may take on a glandular appearance and occasionally eventuate in adenocarcinoma.

The program on June 25 included:

R. A. Burhans, Detroit, described his experiences with perirenal insufflation of air in the demonstration of lesions of the kidney and suprarenal.

S. Lubash, New York City, called attention to the frequency with which renal neoplasms simulate disease of the gastrointestinal tract. Urological investigation and especially pyelography are required in all obscure gastrointestinal complaints.

In discussion Howard Jeck, New York City, warned of severe reactions from perirenal insufflation, and G. W. Fish, New York City, said that he had had two fatalities after using the method safely for eleven years.

F. P. Twinem, New York City, advocates resection of the stone-containing lower calyx of the kidney when the neck of the former is angulated or constricted, and when the calyx is dilated, since such a calyx is likely to serve as a sump in which re-formation of the stone is very probable. Recurrence developed once in ten cases so treated.

R. Chute and H. I. Suby, Boston, stated that infection is a factor in the formation of 50 per cent of renal stones and discussed 66 such cases. In 50 of these an urea-splitting organism was cultured from the urine. Among the urea splitters are: *B. proteus*, *E. coli*, *B. pyocyaneus*, *B. influenzae*, and certain strains of staphylococci and streptococci. Surgical removal was followed by recurrence of the stone in 73 per cent of those infected with organisms capable of splitting urea, and in 23 per cent of those infected with other organisms.

Alexander Randall, Philadelphia, recapitulated his work upon the etiology of nephrolithiasis. He has demonstrated quite conclusively that, in many instances at least, the initial lesion consists of the impregnation, with salts of calcium, of a small area of connective tissue beneath the epithelium of a renal papilla without inflammatory phenomena. Differential staining shows these to consist of carbonates, phosphates, and possibly nucleinates. If the mucosa overlying the plaque peels off, more salts are deposited upon the original nucleus, which may become detached. The calcium is presumably deposited only in damaged tissue, the source of which is as yet unknown.

J. F. McCarthy, New York City, discussed the technique of suprapubic and perineal prostatectomy. He recommended the use in certain poor risks of local anesthesia for transurethral resection. Paraldehyde is given by rectum beforehand; the urethra is cocaineized and 1 per cent procaine is injected directly into the prostate.

The following papers were not heard by the reviewer and are not reported: Presidential Address, J. B. Cross, Buffalo, N. Y.; The Male Climacteric, Its Diagnosis and Treatment, R. J. Douglas, Muskegon, Mich.; The Acute Nonfunctioning Kidney, Stanley R. Woodruff and Wilbert F. Lewis, Jersey City, N. J.; Postoperative Adrenal Insufficiency, F. G. Harrison and H. H. Pote, Philadelphia, Pa.; Hypertension and Hypotension, Their Etiology and Treatment, O. S. Fowler, Denver, Colo.; Periostitis Pubis Following Suprapubic Cystostomy, W. K. Wheeler, Newark, N. J.; Color Photography of the Prostatic Urethra and Bladder, Edgar G. Ballenger, Harold P. McDonald, and Reese C. Coleman, Jr., Atlanta, Ga.; Female Urethral Dilators, the Utilization of an Old Principle, J. Harolde Turner, Houston, Tex.; Diverticulum of the Female Urethra, Its Recognition and Treatment, Frederick J. Parmenter, Buffalo, N. Y.

TESTIMONIAL DINNER TO RUDOLPH MATAS MAY 1, 1940, ST. LOUIS, MO.

AT THE testimonial dinner given for Dr. Rudolph Matas in St. Louis, May 1, 1940, during the meeting of the American Surgical Association, the following speeches were presented:

Irvin Abell, Louisville, Ky., spoke as follows:

"Surgery has a noble heritage. Its disciples are the intellectual descendants of all the great minds who have heretofore charted its course. This assemblage, representative of the ideals and the leadership in American Surgery, comes together tonight to express a tribute of loyalty and friendship, of esteem and regard, of admiration and deference to our honored guest, Dr. Rudolph Matas. In the words of Shakespeare, 'I am no orator as Brutus is,' yet if my hesitating tongue can convey to our guest an appreciation of but a small part of the place he holds in our affection, estimation and confidence, I shall deem it a happy privilege to have participated in this testimonial. To Dr. Matas has been accorded a great favor, that of living through, and taking an active part in, a remarkable transition period in the fruition and development of the art and science to which we bear allegiance. Medical science has made greater progress during his lifetime than in any previous period. Much of the newer work has been created and practically all has been evolved since his student days. Beginning his career in the waning shadow of one school of thought, that founded on clinical observation alone, he has developed it contemporaneously with the growth of modern medicine and surgery, seeing in this golden age the beautifully integrated structure built on scientific, accurate knowledge, to which he has been a constant contributor. Working in his early years without laboratories as we know them and their accompanying refinements in making diagnoses, he acquired what might be termed a compensatory acumen in correctly assessing the value of symptoms, an accomplishment, which, with the advent of the laboratory, aided him in correctly evaluating the clinical and technical aspects of surgical problems, separating the true from the false, the real from the hypothetical, contributing materially to their advancement. The greatest asset possessed by the medical profession is the constantly accumulating fund of knowledge in the minds, the literature and the ideals of its members. The responsibility for its acquisition rests solely

R. C. Yeaw, New York City, studied the effect of pH upon the growth of organisms isolated from the urinary tract and inoculated into media containing urine. Most strains died at a pH of 4.5 without the use of antiseptics. The dangers of acidosis in attempting to attain this level in patients with impaired renal function were emphasized.

Baldwin Lucke, Philadelphia, gave the annual Guiteras Lecture. He related his experiences with a renal adenocarcinoma occurring in frogs. He has studied this tumor sufficiently to establish its "normal" behavior under ordinary circumstances, so that the effect of variations in environment can be evaluated pretty accurately. The tumor can be transplanted to the anterior chamber of the eye or grown in tissue cultures. He found the rate of growth of the tumor roughly proportional to the environmental temperature; i.e., at low temperatures growth was slow. The tumor is due to a filtrable virus.

The following papers were presented on the last day of the meeting, June 27:

E. W. Campbell, Philadelphia, raised again the specter of "sudden emptying of the bladder." He presented the hypothesis that prostates with chronic retention and intrarenal pelvis develop hypertension, and that in these cases sudden emptying of the bladder is dangerous. Convincing proof of the hypothesis was not presented.

E. L. Pierson and S. A. Wilson, Salem, Mass., presented an interesting method of measuring the prostate with the x-ray. A Foley bag is inserted into the bladder, filled with contrast medium, and pulled down onto the upper surface of the prostate. The bladder is then filled with a more dilute medium, and a balloon is inserted into the rectum and also filled with contrast medium. The elevation of the base of the bladder above the pubes, the distance from the base of the bag to the base of the bladder, the distance between the shaft of the bag and the rectal balloon, and the point, in the lateral film, at which the catheter turns forward, indicate the length of the prostate, the degree of intrusion into the bladder, and the thickness of the middle lobe.

C. J. E. Kickham, Boston, reviewed a series of carcinomas of the prostate from the Pondville Hospital. Thirty-nine per cent had extraordinary complaints, usually due to metastasis, at the onset. He favors perineal exposure of the prostate for biopsy in doubtful cases.

B. M. Hance, Easton, Pa., presented a review of fifty suprapubic prostatectomies in good-risk patients without preliminary catheterization, with the object of avoiding infection altogether. The average hospital stay was 15.6 days, less than one-half the usual period.

H. N. Dorman, Washington, D. C., reviewed 300 transurethral resections. He favors preliminary catheter drainage, although it has been proved beyond a doubt that this is unnecessary if the renal function is good and if active infection and complications are absent. No preparation was required by 13.6 per cent, while 1.6 per cent required preliminary cystostomy; 51 per cent remained in the hospital less than a week after operation. His mortality was rather high.

F. E. B. Foley, St. Paul, Minn., presented a new prostatic punch in which the tubular knife is actuated pneumatically. Mr. Frederick Wappler, New York City, showed a colored movie of the punch in action. Power is derived from a cylinder of carbon dioxide. Apparent outstanding advantages are: the speed with which the knife moves facilitates cutting so that it will cut through thick cloth or beef bone; and inertia of the column of water in the sheath expels the excised piece when the knife is retracted.

beyond what the 'Good Book' assigns to man, that beautiful quality of simplicity. Youth takes to this quality like a duck to water; it bridges the years and sets aside all barriers. We cannot recall anyone who has maintained so well this characteristic, as his accomplishments have received recognition.

"You have won for yourself a unique position, and yet in spite of the honors, the medals, the citations, you appear to us, your grandchildren, through the clear light of your simplicity of character, as a man we can still approach—your preservation of modesty and simplicity is an attribute that allows us to come to you, to talk to you, to touch you. It is this characteristic that establishes you firmly in our hearts. Moreover, and to us a chief concern, it is what makes you a good grandfather and a friend to all the world. (What a pity you cannot hand down these essential qualities to some of those who sit in the high places of public life and try to govern us!) Your accomplishments may not be known to all here, and children must be allowed to prattle.

"How many of you here know that in 1879 he served with the Havana Yellow Fever Commission? How many of you know that in every step forward in the public health advances of his beautiful city he was the leader? Possibly all of you know of his great gifts to vascular surgery and of the cure of aneurysm for which he holds world renown.

"But do you know that he was amongst the first to administer spinal anesthesia; that by 1888 his publications covered the topic of replacement of fluid for shock by the continued intravenous drip method; that by 1911 he was advocating gastroduodenal tube siphonage for intestinal obstruction, peritonitis and paralytic ileus? His modesty has allowed others to have their names attached to such life-saving measures though priority of thought and effort belongs to him!

"Grandfather, we salute you! We are happy to be a part of the institution you have founded and so beautifully decorate. In case your children be not sufficiently outspoken, take it from us, your little ones, that you are just right as you are and that we hope you will never change. Certainly no man can detract from what you have done and no man can add to your accomplishments. Like all good grandchildren we leave our affectionate greetings at your feet."

James M. Mason, Birmingham, Ala., also spoke of Dr. Matas as follows:

"It is a happy occasion which brings us together. In the midst of the activities of the meeting of the American Surgical Association, we are invited by our genial host, Dr. Mosby, to spend a social hour in honor of Dr. Rudolph Matas who was the 28th president of the Association, and who is one of its most distinguished members.

"Though long retired from the active work of teaching, and having arrived at that time of life when most men are prone to withdraw themselves from their fellows and to lose interest in current affairs, and to dwell on the 'good old days,' which someone has said, 'never, never were,' Dr. Matas refuses to abide by the rules. He is interested in everything, he reads everything, he sees everything, and is ready at all times to enter into a discussion of any scientific subject which is worthy of a professional gentleman's attention. Instead of being separated from his friends, they seek him out and are drawn closer to him with the passing years. Where in this country, or elsewhere, could he face a more distinguished gathering of his colleagues than now surrounds him? And every one his friend!

"On many occasions, both public and private, I have given expression to my affectionate regard for him; and at appropriate times have outlined the more eventful stops in his career. So long has he wrought among you and so well known to you is his work, that no word that I might utter would add one particle to your knowledge of his accomplishments. Therefore, for my broadcast, you must tune in on a more personal wave length. I claim this privilege by reason of the

on the profession; a duty some are unable to meet, one shirked by others, and one richly fulfilled by those who regard it an unwritten law that they who enjoy the prestige of a profession should enrich it by their efforts and their labors. Dr. Matas has discharged this obligation in fullest measure, finding his reward in a consciousness of service, in the approval and recognition of his confreres, in the satisfaction of his own scientific curiosity and in the gratification that comes from contributing to the common fund from which all may draw. His career and his achievements furnish inspiration and in whatever aspects they may be viewed afford an example worthy of our admiration and limitation. The biblical adage states that 'By their fruits shall ye know them.' A profound thinker, a brilliant operator, a renowned teacher, a distinguished author, a contributor of original work increasing the sum total of medical knowledge, an artist evincing a culture of superlative dimensions, he possesses attributes constituting the fruits by which we know him and which fully justify our saying with the Latin poet 'He has builded a monument more lasting than brass.' For the vast majority of us life's stream pursues its tranquil course ending in the ocean of oblivion without its power, its beauty or its strength having established a landmark that would differentiate it from those of our contemporaries. To possess the culture, education, intellectuality and ability, to have maintained the highest standard of professional and ethical excellence, to have lived a life of service in one's community and nation and to have displayed loyalty to ideals in a degree to win and merit the multitude of honors that have been showered upon him by the profession of the world is to stamp the recipient of such honors as a man among men, and as a surgeon among surgeons. These honors and preferments so richly bestowed are but the visible proof of the influence he has had on scientific medicine. I once heard Dr. William J. Mayo quote an old Persian proverb to the effect that 'he who learns and learns and yet does not what he knows is like the man who plows and plows but never sows.' Dr. Matas is one who has learned and learned and sown and sown, sown deeply in the fertile field of practice with the result that during a long career a veritable multitude has arisen to call him blessed. To those who have been privileged to bask in the sunshine of his friendship he has ever been a delightful companion, a friend who knowing us as we are loves us still, an unexcelled exemplar of the humanities and the amenities. I confess, Dr. Matas, that only under the conditions afforded by this testimonial would we so unreservedly bare our hearts to you, fearing that our seeming boldness might have an undesirable reaction on your sense of propriety. You deserve the encomiums and the praise given you this evening, and if they prove somewhat disconcerting, I trust you may be able to say of them, as the maiden said of her first kiss, somewhat embarrassing, but after all most enjoyable."

Elliott C. Cutler, Boston, presented the following:

"I welcome the opportunity to share in this happy occasion surrounded by such devoted followers of our honored guest, followers well endowed with oratorical abilities. I have, indeed, wondered what small part I might claim as my own tonight.

"It is clear from the shiny domes and whitened temples, that if our younger members will permit and will acknowledge my lack of the above physical attributes, I can speak for them. I speak therefore not as a child of the Matas tradition but a grandchild.

"We, your grandchildren, Rudolph Matas, salute you! We take great pleasure in recording our deep appreciation of permitting us to partake of this inheritance and we in our toddling days find in grandfather all the fine qualities which men admire and emulate. And you, grandfather, have chiefly preserved, to years well

"At the dinner in his honor at the recent sectional meeting of the American College of Surgeons in New Orleans, it was my privilege to make one of the addresses.

"The crowning glory of his professional life, and certainly the most interesting experience which has ever come to me, was the meeting of the International Surgical Society over which he presided in Brussels in 1938. The opening meeting was held in the hall of the Belgian senate, where were gathered representatives of the King, noted city and state officials, including Burgomaster Max, who along with Cardinal Mercier and other heroic Belgians, was imprisoned during the German occupation, and representatives from forty countries. Dr. Matas addressed this assembly in classic French, the language of diplomacy throughout the world. Following this he presided with such grace and dignity at all the sessions of the society that he filled the hearts of the American delegates with pride, and placed American surgery on a plane which challenged the admiration of the world!

"Each night he attended elaborate social functions; and as a gracious courtesy to Dr. Elliott Cutler, the American Secretary of the society, and to the eighteen or twenty American delegates, he gave an elaborate luncheon which none of us will ever forget.

"Following the adjournment of this meeting, we spent a week in Paris. It was the week before 'Munich.' England, France and Germany were on the point of declaring war. Ambassador Bullitt was urging all Americans to go home. The steamship offices were crowded with people seeking passage. Those who had no reservations were frenzied with anxiety. Members of his family who were with him were imploring Dr. Matas to return home with them, but he was unperturbed and stayed on. Absolutely the most unexcited individual in Paris at the period of greatest tension, his attitude reminds one of that of the village preacher so beautifully described by Oliver Goldsmith in his *Deserted Village*, of whom he says:

'As some tall cliff which lifts its awful form,
Swells from the vale and midway leaves the storm,
Though round its breast the rolling clouds may spread,
Eternal sunshine settles on his head.'

And so he stayed on. The war clouds rolled away for a time, and he brought back to us the most vivid and interesting accounts of War surgery in Spain that have reached us.

"It was while relating his observations at the meeting of the Southern Surgical Association last December, that my candid camera caught him in the very characteristic pose which you find on your place cards this evening."

fact that Dr. Matas and I have come along together. In 1895 he began to teach surgery at Tulane, and in the same year, I began to study surgery at the same school. He was at the top of the ladder; I was at the bottom. In the intervening years, our relative positions have remained unchanged.

"At this period he was at the height of his activity in the development of modern vascular surgery, and it was hardly a coincidence that on the occasion of my first contact with him in ward rounds, he was engaged in demonstrating to a group of students the MacEwen operation of needling a subclavian abscess. In later years, on more than one occasion, I have spent strenuous minutes which seemed like hours, as the entire intern staff of the Charity Hospital, in relays, made digital compression on the femoral artery in worthy but, as I recall them, futile attempts to improve the condition of aneurysms of the lower extremity. On behalf of all the interns that have succeeded me, I thank you, Dr. Matas, for the mechanical compressor which you have since devised.

"Though following him as carefully as I could, and assisting at his operations whenever I might, I have always felt that my internship was lacking in completeness in that, as rotation in the hospital carried us from ward to ward, I was never assigned to his service. I well remember his successful handling of an interesting colloid carcinoma of the omentum, and many of the interesting operations which he performed in those early days under local anesthesia. On one particular occasion I may have been of some material help to him. He was operating on a large uterine fibroid at one of the smaller hospitals of the city, and had the misfortune, which may at times befall the greatest of surgeons, to encounter serious complications in a difficult case and find himself short handed for assistants.

"When Dr. Matas spied me in the operating room corridor, he called for help, and I have always felt that he was glad to have me lend a hand.

"And that reminds me of another great surgeon who got into difficulties. A few years before World War No. 1, I was spending some time in Berlin, and, in company with some other Americans, visited the gynecological operating room of Professor Bumm at the Charite. The amphitheater was filled with three or four hundred German students, and we saw on the operating table a woman whose abdomen was distended with what was most probably an ovarian cyst. To confirm the diagnosis which we had made by inspection, and at long distance, the Professor wrote upon the blackboard the name, Ephraim McDowell, and 1809, the date of his first ovariectomy. He then recounted to the students the history of McDowell's celebrated operation, and praised the heroism and fortitude of his patient, Mrs. Crawford. We felt very proud of America!

"Next, he made a Pfannenstiel incision, very popular at that time; but instead of finding a simple freely movable ovarian cyst with an easily accessible pedicle, such as McDowell had the good fortune to encounter, he got into an adherent, suppurating broad ligament cyst. We spent an hour watching him and his assistants clamp, sponge, aspirate and ligate, but had to leave before the finish. We left feeling very sorry for Germany! When we see these things happening in high places, just as they often happen to many of us, we are again reminded that even among surgeons, 'Judy O'Grady and the Colonel's Lady are sisters, so to speak, under the skin.'

"Since my student days it has been my good fortune to come in contact with Dr. Matas at meetings of this and other scientific societies. I was permitted to take part in the exercises which attended the presentation of the 'Birthday Volume'; and he has been an interesting and honored guest in my home, where he captured all hearts.

dogmatism is beneficial when the reader is a student of the subject, but may leave the casual peruser with a prejudiced viewpoint. The bibliography is excellent. Except for twenty counted typographical errors in spelling, the book is well printed and easily readable.

Infections of the Hand. By Allen B. Kanavel, M.D., Late Professor of Surgery, Northwestern University Medical School, Chicago, Ill. Ed. 7. Cloth. Pp. 503, with 229 illustrations. Philadelphia, 1939, Lea and Febiger. \$6.

Early in his career, the late Allen B. Kanavel set himself the task of understanding the minute anatomy of the hand. Out of that ambition grew the most authoritative surgical monograph on the infections of the hand extant. The present seventh edition was printed after Dr. Kanavel's untimely death.

The major emphasis, as in previous editions, has been on the anatomy of the hand. Employing injection techniques, Kanavel was able early to indicate the manner in which infections spread in the hand and fingers. All those engaged in the practical aspects of the management of hand infections of necessity must familiarize themselves with Kanavel's postulates. An appropriate chapter on reconstructive procedures for the sequelae of hand infections is appended.

Kanavel left in Chicago, the site of his surgical activity, a number of disciples who have carried on and extended the Kanavel tradition. It is to be hoped that this book will continue to live in new editions through their interest.

Dr. Kanavel came from the anatomic school. Appropriately, the anatomy of the hand as related to surgery has been given paramount emphasis. In subsequent editions, the bacteriology of infections, as related to chemotherapy and a more detailed physiologic consideration of the therapeutic value of nonoperative measures, will probably be given greater emphasis.

A Synopsis of Surgical Anatomy. By Alexander Lee McGregor, M.D. Ed. 4. Cloth. Pp. 664, with 648 illustrations. Baltimore, 1939, William Wood & Company. \$6.

The author has succeeded in presenting in an interesting manner many anatomical facts of practical importance. No attempt, however, to cover the whole field of surgical anatomy has been made. This detracts a great deal from the value of the book and is the chief criticism which can be made of it. A consideration of the anatomy of the brain, with the exception of that of the pituitary gland, is entirely omitted. There is no consideration of the arterial system, although the veins are discussed at length. Various organs, such as the lungs, stomach, pancreas, and spleen, have been neglected.

The book is divided into two main parts. In the first part certain normal anatomical relationships are set forth. In the second part the anatomy of various pathologic conditions is outlined. In many chapters the narrow bounds of descriptive anatomy are overstepped and the anatomic basis for the pathologic physiology of many diseases is indicated.

Throughout the book emphasis is continually placed on the practical value of a knowledge of anatomy. The text contains frequent hints which are supposed to aid in the memory of important relationships. There is an abundance of illustrations and diagrams in each chapter. The last two chapters of the book, "The Anatomy of Surgical Procedures" and "The Anatomy of Surgical Approach," comprising some seventy pages, more properly belong in a textbook of surgery. The information contained therein, however, is valuable.

Book Reviews

Shock and Related Capillary Phenomena. By Virgil H. Moon, A.B., M.Sc., M.D., Professor of Pathology, Jefferson Medical College. Cloth. Pp. 442, with 29 illustrations and 5 charts. New York, 1938, Oxford University Press. \$3.50.

Moon's book approaches the subject of shock from the viewpoint of the pathologist. While this angle of approach is by no means novel, it has been much neglected of late, especially in the American literature.

This book is bound to be of interest. It is the first monograph on shock in any language for fifteen years (the last being Cannon's book in 1923). In the first portion of the book is one of the most complete reviews of capillary phenomena extant. The work of Krogh, Ebbecke, Landis, Lewis, Menkin, and others in this field is analyzed and correlated. The importance of the wheal is emphasized.

The next, and middle, part of the book develops the thesis that the wheal is shock in miniature. This portion of the book introduces the reader to the idea already expressed in the title that shock is a capillary phenomenon. The author's well-known definition of shock is given: "Shock is defined as a circulatory deficiency not cardiac nor vasomotor in origin, characterized by a decreased volume of blood, reduced cardiac output (volume flow of blood) and by hemoconcentration." While admitting that the hemoconcentration which sets off the rest of the train of events is partly caused by local fluid loss, emphasis is placed on a generalized fluid loss due to action of substances similar to those which produce wheals locally, namely, the products of trauma. This brings forth the old toxic theory of Cannon in a new and better fitting dress and represents an advance in viewpoint. On the other hand, the chief evidence presented for this theory is qualitative rather than quantitative. Furthermore, much of the qualitative evidence is based on terminal pathologic findings and may represent merely the results of late anoxia rather than of early action of tissue metabolites. From a practical standpoint, it seems as though the separation of hemorrhagic shock from other types is made too much to fit the above definition of shock; i.e., accompanied by hemoconcentration. Little distinction is drawn between the effects of rapid and prolonged hemorrhage. Not all surgeons would agree with the statement on page 88 that "it is well established in the etiology of osteomyelitis that the infection is usually preceded by a slight injury, such as a bruise, a wrench or a strain."

The third, and last, portion of the book considers various clinical conditions in which a shocklike syndrome may occur. This is one of the best sections. This reviewer was especially struck by the concept that many of the post-mortem findings usually denoted as due to "passive congestion" or to "terminal bronchopneumonia" are in reality due to a generalized outpouring of fluid caused by some shocklike condition. To quote only one example, it is postulated that many instances of postoperative pneumonia may be due to development of a sublethal degree of shock, a type of "hemorrhagic edematous pneumonia" being of very common occurrence if neither death nor recovery occurs too soon.

This book can be heartily recommended to physiologists, pathologists, and those in the preclinical sciences. It correlates many of their observations from a clinical viewpoint. The first and third portions of the book can be recommended unreservedly to clinicians. The middle portion is an excellent, even though one-sided, exposition of the "toxic" theory of shock. Criticisms of other writers often do not pay enough attention to the context of the cited material. Possibly this very

Part IV contains four lectures grouped under the general title, "Some Approaches to the Nervous Control of the Organism." Titles and authors are as follows: "The Physicochemical Approach to the Mechanisms of Convulsive Reactivity" by Irvine McQuarrie; "Methods of Analysis of Nervous Action" by Herbert S. Gasser; "The Nervous Regulation of Visceral Processes" by Detlev W. Bronk; and "The Argument for Chemical Mediation of Nerve Impulses" by Walter B. Cannon.

It is not feasible to review adequately each lecture because the material presented is condensed and pertinent to the subject. While all the addresses should be of interest to physiologists, biochemists, and individuals interested in recent advances relating to scientific medicine, Parts II and III contain material of special value to the clinician. The fields included in the lectures in Parts I and IV are necessarily encumbered with specialized and technical terms which in most articles on the subjects make understandable reading by an individual not familiar with the subject all but impossible. The articles on these subjects in this volume are characterized by a simplicity of expression which a master of a subject sometimes achieves and thus convey meaning to the technically uneducated reader. The volume is adequately provided with simple illustrations.

Synopsis of Operative Surgery. By H. E. Mobley. Pp. 375, with 339 illustrations, 39 color plates. St. Louis, 1940, The C. V. Mosby Co., \$4.50.

The author has attempted to present concisely "the fundamental principles of operative technique" in a pocket-size edition. The various steps in the operative procedures are briefly described "in logical sequences" and illustrated with simple pen-and-ink drawings.

The first few chapters are devoted to preparation of the patient and surgeon for operation, anesthesia, postoperative care, knot tying, and incisions. The remaining chapters deal with surgical procedure applicable to various regions of the body. The value of this fairly comprehensive synopsis is unfortunately marred by certain inaccuracies and the author's apparent lack of familiarity of some of the present-day operative methods. Certain procedures, which in recent years have become fairly standard, are conspicuous by their absence and others, which are now more or less obsolete, by their presence. Thus, for example, sympathetic block, sympathectomy, and transverse abdominal incisions are not even mentioned. On the other hand, vessel anastomosis, radical phlebectomy for varicose veins, direct transfusion, neuroplasty, and gastropexy are prominently described and illustrated. Moreover, the descriptions and illustrations of some of the procedures seem to follow rather antiquated texts, as, for example, the procedure of thoracoplasty and the anterior approach to the liver. Some of the illustrations are obviously incorrect, such as that of phrenicectomy, showing the phrenic nerve coursing across the scalenus anticus muscle obliquely downward and laterally and the technique of hypodermoclysis showing the needles inserted directly beneath the breasts. The book is, however, compact and very readable.

The Fundamentals of Internal Medicine. By Wallace Mason Yater. Ed. 1, Pp. 1,021, with 254 illustrations. New York, 1940, D. Appleton-Century Co. \$9.

Fifteen months after the first edition of this volume appeared, a revised edition has been published. In the preface to the first edition the author stated that his purpose was to present in simple form a book for students and practitioners containing the essentials of internal medicine. It was an answer to the complaints

Fractures, Dislocations, and Epiphyseal Separations. By Harry C. W. S. deBrun, M.D., F.A.C.S. Cloth. Pp. 468, with 150 illustrations. Chicago, 1939, The Year Book Publishers. \$3.

This is a concise, well-written outline of fractures, dislocations, and epiphyseal separations which will prove to be a valuable handbook to the general practitioner and especially for interns and surgical house officers. It is obviously not intended for those specializing in the treatment of fractures or orthopedics.

The material is presented largely in outline form. In most cases several forms of treatment are listed; e.g., in fractures of the os calcis four methods are described. Yoerg's procedure is unfortunately omitted. Forceful hyperextension methods of reducing compression fractures of the lumbar spine are also omitted. There is no mention of the use of vitallium for the internal fixation of fractures.

Illustrations and roentgenograms of necessity are limited in number. The illustrations of the fracture equipment setup will prove valuable ready references for interns and surgical house officers. There is a short chapter on physiotherapy and a valuable discussion on the roentgenologic diagnosis of fractures is included.

Chemistry and Medicine. Edited by Maurice B. Visscher, Professor of Physiology, Medical School, University of Minnesota. Cloth. Pp. 296, with 73 illustrations. Minneapolis, 1940, University of Minnesota Press. \$4.50.

This volume consists of fourteen lectures which were delivered as a part of the program commemorating the fiftieth anniversary of the founding of the Medical School of the University of Minnesota, Oct. 12, 13, and 14, 1939. The subjects of the lectures are related to a single general theme, "Some Trends in Medical Progress With Particular Reference to Chemistry in Medicine." This theme was chosen because it represents one of the most recently developed and more rapidly expanding aspects of medical science. Each lecturer was selected on the basis of his special fitness to present an authoritative address on the chosen subject. The fourteen lectures were edited by Maurice B. Visscher, Chairman of the Anniversary Committee on Publications.

The nature and scope of the material included in the volume can be indicated by the method of organization of the monograph and the listing of the titles of lectures and authors. The entire subject material is divided appropriately into four parts.

Part I consists of three lectures dealing with related phases of the general subject, "Progress in the Application of Physical Chemistry to Medicine." The first lecture is by Herbert Freundlich on "Some Aspects of the Colloid Chemistry of Membranes," the second by Maurice B. Visscher on "The Performance of Osmotic Work in Living Systems," and the third by John P. Peters on "Some Reactions by Which Solutes May Be Differentially Concentrated by the Kidney."

Part II contains three lectures dealing with the general subject, "Some Recent Investigations in Metabolism." Subjects and authors are as follows: "Organic Chemistry in the Pursuit of Vitamin Research" by Lee Irvin Smith; "On the Necessity of Fats in the Diet" by George O. Burr; and "Heparin and Thrombosis" by Charles H. Best.

Part III deals with "Some Aspects of Immunity and Chemotherapy" and consists of four subjects very pertinent to this theme: "Recent Chemical Trends in the Study of Immunity" by Michael Heidelberger; "The Biology of Animal Viruses" by Robert G. Green; "The Mode of Action of Sulfanilamide and Its Derivatives" by Perrin H. Long, and "Chemistry in Urinary Antisepsis" by Henry F. Helmholtz.

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PARTIAL GASTRECTOMY FOR PEPTIC ULCER

A REVIEW OF SEVENTY-FOUR OPERATIONS

ROY D. McCLURE, M.D., AND LAWRENCE S. FALLIS, M.D.,* DETROIT, MICH.
(From the Department of Surgery, Henry Ford Hospital)

FOR many years the operative procedure at the Henry Ford Hospital for peptic ulcer, apart from perforation, was limited to gastroenterostomy. Our results in general were good so far as immediate benefit was concerned, but many of these patients continued to have recurring attacks of gastric distress which limited their activity and in some instances led to a state of chronic invalidism. Marginal ulcer, the *bête noire* of the gastric surgeon, has been in our experience a rare sequela of gastroenterostomy. We believe that freedom from this and other serious complications has been due to following the operative technique taught to one of us (R. D. M.) by Finney.¹ This procedure employs the Halsted² principles of no crushing clamps, a minimum of catgut sutures, and the use of fine silk on atraumatic needles for the approximation of the serosal and submucosal coats. Our experience with gastroenterostomy in the treatment of peptic ulcer agrees with that of other observers in that the best results are obtained in long-standing cases of pyloric ulcer with organic stricture and definite maintained gastric retention which does not yield to conservative treatment. Gastroenterostomy is not satisfactory in the treatment of peptic ulcer when pyloric obstruction is intermittent, since this indicates that the blockage is due to the edema of pronounced hyperacidity with accompanying gastritis and duodenitis.

Dissatisfaction with the end results of gastroenterostomy led us into a brief trial of the so-called physiologic operations on the pylorus. Of these, the Finney pyloroplasty³ is best because it is more radical than the limited pyloroplasty of the Heineke-Mikulicz or Horsley type.

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*The authors are indebted to Dr. J. Risk Meek for valuable assistance rendered in the preparation of this material.

of students "that they 'can't see the woods for the trees.'" It was his hope that as the student progressed he would consult more comprehensive systems and textbooks of medicine and original articles. The publication of a new edition in such a short space of time is the result of an agreement on the part of the author and publisher to keep the material up to date.

The contents of the volume have been presented in an unique and effective manner. The book is divided into several sections. Each section is headed by an outline of the topics that are to be discussed. Important statements and key words are presented in bold type. The outline form is used frequently throughout the book. In discussing the pathogenesis of disease processes, due regard has been given to physiologic and pathologic considerations. Another feature of this work not found in many textbooks of medicine is the large number of well-reproduced illustrations. Several of the sections have been written in collaboration with outstanding authorities in their fields. Among these is Dr. Sanford Rosenthal, Senior Pharmacologist of the National Institute of Health, who contributed sections on "The Diseases Due to Intoxications," and "Diseases Due to Physical Agents." Dr. W. H. Sebrell, Surgeon of the National Institute of Health, collaborated on "Diseases Due to Vitamin Deficiency." Some exception might be taken to including sections on "Diseases of the Skin," "Diseases of the Ear," and "Diseases of the Eye" in a textbook of internal medicine. However, the section on "Diseases of the Skin" is excellent. In the copy available for this review two pages of the index have been omitted in publication.

The material as a whole is orthodox and well presented. In an attempt to present only the fundamentals of internal medicine, perhaps some topics are inadequately discussed, while other subjects are given more space than they warrant. As an example, the same amount of space is devoted to a consideration of sickle-cell anemia as is given to a general discussion of allergy. While the author and publishers are to be commended for their endeavor to keep the material up to date, recent therapeutic procedures are included which have not been, and perhaps will not be, generally accepted. In discussing the use of sulfamido compounds for staphylococcal septicemia the following statement is made: "One that appears to be of considerable value in staphylococcal septicemia is a methylated derivative of sulfathiazole known as sulfamethylthiazole, administered in similar dosage to sulfapyridine. It is apparently less toxic than the latter." Subsequent investigations have shown that sulfamethylthiazole is quite toxic, and it is doubtful that it will be available for general use.

Yater has accomplished his task well. The volume can be recommended for the student entering upon the study of clinical medicine for the first time as well as the surgeon who desires a concise summary of recent advances in internal medicine.

TABLE I
AGE DISTRIBUTION

| DECADE | AGE | NUMBER OF CASES | PERCENTAGE |
|--------|-------|-----------------|------------|
| 3rd | 20-29 | 4 | 5.4 |
| 4th | 30-39 | 19 | 25.7 |
| 5th | 40-49 | 25 | 33.8 |
| 6th | 50-59 | 18 | 24.3 |
| 7th | 60-69 | 8 | 10.8 |
| Total | | 74 | 100.0 |

Youngest patient, 22 years; oldest, 67 years; average, 44.7 years.

difference in the daily life of the sexes and the excessive stress and strain to which men are subjected as compared with women. Most will agree that this is an important etiological factor in the production of ulcer, and certainly these figures would tend to substantiate this opinion.

Race Distribution.—Over 90 per cent of the patients were white, and, since in this area the colored population is 7.2 per cent of the total, there is apparently no racial immunity.

TABLE II
OCCUPATION

| GROUP | NUMBER OF PATIENTS | PERCENTAGE |
|----------------|--------------------|------------|
| Laborer | 40 | 54.2 |
| "White-collar" | 15 | 20.2 |
| Executive | 12 | 16.2 |
| Professional | 7 | 9.4 |
| Total | 74 | 100.0 |

Occupation.—Table II shows the division of these patients according to occupation. The relatively high proportion of patients in the "executive" and "professional" groups again brings up consideration of stress and strain as important etiological factors. These two groups, together with the "white-collar" group, almost equal the number of the laboring group, although they are far outnumbered in the general population.

CLINICAL FEATURES

The subjective symptoms of peptic ulcer are characteristic and are of great diagnostic value.

TABLE III
LOCATION AND CHARACTER OF PAIN

| | |
|-------------------|------|
| Pain | 85.2 |
| Epigastric | 78.4 |
| Not located | 6.8 |
| Burning | 14.8 |
| Fullness | 13.6 |
| Gnawing | 10.8 |
| Not characterized | 45.9 |
| No pain | 14.8 |

All figures indicate percentages.

We have had no experience with direct gastroduodenostomy as sponsored by von Haberer⁴ in Germany and Wilkie⁵ in Scotland because results, except in the hands of the sponsors, have not been entirely satisfactory. The chief difficulty, as Wilkie has pointed out, has been in the failure to secure adequate mobilization of the duodenum, a point that has been so frequently stressed by Finney.⁶ However, even in the European strongholds of this operation, the tendency has been to abandon it in favor of partial gastrectomy. Wilkie, just before his untimely death, had given up gastroduodenostomy because of the high incidence of marginal ulcers that appeared in his patients whose cases were followed over a period of years.

Beginning with pylorectomy, we have gradually extended this operation until our present-day operation of partial gastrectomy implies removal of from two-thirds to three-quarters of the stomach. This shift to the left, to borrow the phraseology of Connell,⁷ has not been accepted without some misgivings. The surgeon who advises such an extensive operative procedure as partial gastrectomy for such a small lesion as duodenal ulcer must believe wholeheartedly in the operation. His beliefs must be founded on facts, preferably drawn from his own observations and experiences. It was on this basis that our decision to continue with partial gastrectomy as the operation of choice for peptic ulcer was formed.

The patient who faces a formidable operation has two questions foremost in his mind. First, what are my chances of surviving the operation; and second, do I have a reasonable chance of being relieved of my present distress? To the former question, we reply that the mortality rate during the past five years has been 5.3 per cent and that the last thirty-four consecutive ulcer patients who were submitted to partial gastrectomy have all survived; and to the latter question we reply that a satisfactory result has been obtained in approximately 90 per cent of the cases.

The material for this study was taken from the records of the Henry Ford Hospital and includes the case histories of seventy-four consecutive patients with partial gastrectomies performed during the approximately five-year period, Jan. 1, 1934, to March 1, 1939.

Age Distribution.—The youngest patient in the group studied was aged 22 years, and the oldest was aged 67 years. The average age of 44.7 years is higher than is usually given for ulcer patients, since the average patient had been a victim of peptic ulcer 7.5 years before submitting to operation. The age by decades is shown in Table I in which again the advanced age of the patient is emphasized, for 70 per cent of them were over 40 years old and 35 per cent were over 50.

Sex Distribution.—Males outnumbered females in the proportion of nine to one. The high incidence of ulcers in males brings out the great

TABLE IV
ROENTGENOGRAMS

| DIAGNOSIS | NUMBER OF PATIENTS | PERCENTAGE |
|-----------------------------|--------------------|------------|
| Duodenal ulcer | 42 | 56.80 |
| Gastric ulcer | 19 | 25.70 |
| Narrowed or deformed antrum | 5 | 6.70 |
| Marginal ulcer | 3 | 4.05 |
| Gastrojejunal ulcer | 1 | 1.35 |
| Jejunal ulcer | 1 | 1.35 |
| Negative | 1 | 1.35 |
| Not recorded | 2 | 2.70 |
| Total | 74 | 100.00 |

X-Ray Examination.—Table IV shows the results of the six-hour and immediate x-ray examination of the stomach. A definite localized diagnosis was made in almost 90 per cent of these patients. The diagnosis was qualified in only five patients. Only one patient was entirely negative to x-ray. The two not recorded were patients with hemorrhage. This record shows very clearly the importance and accuracy of the x-ray diagnosis. The necessity of a repeated examination whenever there is any question about the certainty of the x-ray findings is generally recognized.

TABLE V
DURATION OF SYMPTOMS BEFORE OPERATION

| LENGTH OF TIME | NUMBER OF CASES | PERCENTAGE |
|--------------------|-----------------|------------|
| Less than 6 months | 8 | 10.8 |
| 6 mo. to 2 years | 15 | 20.4 |
| 2 yr. to 5 yr. | 9 | 12.2 |
| Over 5 years | 42 | 56.6 |

Longest period, 20 years; shortest, 2 weeks (bleeding ulcer); average, 7.5 years.

Duration of Symptoms Before Operation.—A study of Table V serves to emphasize our attitude toward operation, for here it is shown that the average patient suffered from ulcer symptoms for 7.5 years before being subjected to operation. Two-thirds of the patients had characteristic remissions of their ulcers in periods varying from one month to seven years with an average remission period of six months. Despite the patients' being subjects of a chronic annoying condition, the actual period of disability before operation was relatively short, averaging only twenty-four days for the group and ranging from one day in a bleeding ulcer patient to six months.

Selection of Patients for Operation.—Ulcer patients become candidates for partial gastrectomy only when adequate medical treatment has failed. All the patients in this series were subjected to operation only after conference between one of us and Dr. John Mateer or Dr. James Baltz of our Gastroenterological Division. The following are our definite indications for operation: (1) Cicatricial pyloric obstruction, (2) perforating type of ulcer, usually into the head of the pancreas, (3) as a lifesaving measure in persisting acute hemorrhage, (4) history of re-

Pain.—Pain was by far the most constant symptom; 85 per cent of the patients had this complaint. Table III outlines the details of this complaint. Thirty-five per cent had no regularity in the time of occurrence of the pain in relation to meals. Forty-nine per cent had pain from one to three hours after eating. Eleven per cent had pain less than one hour, and five per cent three hours, after eating. Only 17.5 per cent of the patients complained of night pain.

Nausea and Vomiting.—Nausea and vomiting was described as frequent by 28.5 per cent of patients; by 31 per cent as occasional; and by 11 per cent as rare. Thirty-nine per cent had no nausea or vomiting. Eighteen patients, or 24 per cent, noticed blood in the vomitus, and 30 per cent noticed blood in the stool.

Weight Loss.—This was not a prominent feature, since it occurred in only 27 per cent of these patients. However, the average loss was 21 pounds in six months. Apparently the weight loss was either very pronounced or did not occur.

Anemia was noted in only 36.5 per cent of the patients.

Physical findings are of little help in establishing the diagnosis of peptic ulcer and are of much less significance than the history and symptoms. Only 8 per cent of the patients showed general debility. Thirty-six per cent were recorded as showing pallor; 42 per cent had tenderness in the epigastrium, and only 13 per cent had more than slight tenderness. Eight per cent had muscle spasm. Eighteen per cent showed evidence of sinus disease. This is a significant figure and bears with the contention that sinus infection may be important as a focus of infection in the production of an ulcer. The average blood count was 4,200,000, with hemoglobin, 81 per cent. The hemoglobin and urinary findings were relatively unimportant, over 86 per cent being entirely normal.

Gastric Analysis.—As generally recognized, gastric analysis findings usually are not of importance or value in establishing the diagnosis of uncomplicated peptic ulcer. However, in the diagnosis of early pyloric obstruction, the overnight retention of food in the stomach confirms the significance of the six-hour barium retention in the stomach. In the second place, knowledge of the general level of free acidity in a patient with peptic ulcer is essential in the previous medical management, first, because it aids in determining the amount of alkali indicated, and, second, in the case of gastric ulcers, if a marked subacidity is found, because it is one point suggesting that the possibility of a malignant type of ulcer should be kept in mind especially.

The well-known terminal rise of free acidity was noted in a number of the duodenal patients, although many of them had a free acidity within normal limits. It might be of interest to note that all of the duodenal patients in this group who exhibited a definite hyperacidity obtained excellent results from partial gastrectomy.

TABLE VII
TYPE OF OPERATION

| | NUMBER OF CASES | PERCENTAGE | COMPLICATIONS | DEATHS |
|----------------------|--------------------|------------|---------------|--------|
| Polya | 60 | 81.10 | 19 | 4 |
| Finsterer | 7 | 9.50 | 3 | 0 |
| Billroth II | 5 | 6.70 | 1 | 0 |
| Subtotal gastrectomy | 1 | 1.35 | 1 | 0 |
| Sleeve resection | 1 | 1.35 | 0 | 0 |

anastomosing only the lower portion is of definite value in deflecting the upper intestinal contents past the stoma rather than cascading it into the stomach, as occurs with the Reichel-Polya operation. This impression has been confirmed on many occasions by noting that there is a great deal less bile aspirated by the continuous suction tube when the Hofmeister-Finsterer technique is employed. It has also been our experience that this valve formation delays the appearance of bile in the suction tube by at least twenty-four hours, for with the Reichel-Polya operation bile usually appears on the second postoperative day, while with the Hofmeister-Finsterer modification, bile is often not present until the third postoperative day. We believe that the first bile tends to be deflected along the jejunum past the gastric stoma and that bile appears in the stomach only when the full flow returns. The appearance of the bile in the gastric suction tube after partial gastrectomy is a welcome sign indicating that all is well with the duodenal closure, for we have come to believe that duodenal blowouts are caused more by obstruction between the duodenum and the gastric stoma than by faulty technique in closure of the duodenal stump. We have also noted that, since adopting the Hofmeister-Finsterer technique, our patients have not complained of occasional regurgitations of bile, a complication which not infrequently occurs during the convalescence following the Reichel-Polya operation. While only seven of the patients included in this study were subjected to the Hofmeister-Finsterer technique, the foregoing impressions are based upon an experience of twenty operations of this type. We favor the retrocolic, isoperistaltic plan of gastrojejunal anastomosis, using only just enough jejunum to reinforce the closed upper portion of the stomach without distortion of the intestine. Care is exercised to place the anastomosis in the infracolic compartment to avoid constriction of the efferent loop of the jejunum.

Pathologic Diagnosis.—Table VIII records Dr. Frank Hartman's diagnosis of the resected specimens. Duodenal ulcers outnumber gastric ulcers nearly two to one in this series. This is due partly to the much greater incidence of duodenal ulcer, partly to the greater incidence of repeated recurrences and chronicity in duodenal ulcer, and, finally, to the fact that duodenal ulcer is more likely to cause pyloric obstruction either reflexly by developing inflammatory edema or by contracture de-

peated hemorrhages, (5) suspected malignant type of gastric ulcer, (6) gastrojejunal ulcer, and (7) recurrent ulcer activity after comprehensive and adequate medical treatment.

There are the following *relative* indications: viz., (1) patients in the lower economic group who cannot afford financially to follow out medical treatment properly and to face, then, possible subsequent surgical treatment; (2) patients whose intelligence quotients will not permit them to follow a medical program of therapy accurately; and (3) patients with a major type of nervous problem which is likely to interfere with successful medical treatment.

Anesthetic.—During the past year, spinal anesthesia has been used almost exclusively. Nupercaine administered by the Jones⁸ technique provides adequate anesthesia lasting well over two hours. Blood pressure is more readily maintained at normal levels, and there is less nausea and vomiting with dilute solution of nupercaine, 1:1,600, than with the higher concentrated spinal anesthetic agents. Furthermore, it has not been found necessary to augment the spinal nupercaine with splanchnic injections. The calm, peaceful condition of the spinal anesthetic patients both in the immediate postoperative period and on the following day is in marked contrast to the usual postanesthetic condition of the patient who has had a general anesthetic. Chest complications are especially serious after general anesthesia; pulmonary affections are definitely less after spinal anesthesia, although atelectasis is just as frequent. It is significant to note that in Table VI there were no deaths in

TABLE VI
ANESTHETICS

| AGENT | NUMBER OF CASES | PERCENTAGE | DEATHS |
|--------------------|-----------------|------------|--------|
| Ethylene and ether | 56 | 75.65 | 4 |
| Ethylene | 4 | 5.40 | 0 |
| Spinal | 14 | 18.95 | 0 |
| Total | 74 | 100.00 | 4 |

the patients to whom spinal anesthesia was administered. The group considered in Table VI is small, but we have now performed forty consecutive partial gastrectomies under spinal anesthesia, with only one death, and that not due in any measure to the anesthetic agent.

Type of Operation Performed.—In the evolution of the operation of partial gastrectomy as developed by the authors, there has been a gradual trend toward more radical operations until now we feel that it is necessary to remove from two-thirds to three-fourths of the stomach in order to obtain the best results. The type of operation has changed too, as indicated in Table VII, from the Billroth II⁹ to the Reichel-Polya,⁹ and more recently to the Hofmeister-Finsterer⁹ technique. The latter operation is now regularly performed because we consider that the valve formed by closing the upper end of the sectioned stomach and

vents any collection of fluid in the stomach. The various complications as they occurred in the patients of this series are tabulated in Tables IX and X. Two tables have been compiled in order to demonstrate that

TABLE IX
EARLY COMPLICATIONS OF OPERATION

| | NUMBER OF PATIENTS | PERCENTAGE OF TOTAL |
|--------------------|--------------------|------------------------|
| Atelectasis | 13 | 17.5 |
| Ileus | 12 | 16.2 |
| Shock | 7 | 9.5 |
| Pneumonia | 5 | 6.8 |
| Peritonitis | 4 (4 fatal) | 5.4 |
| Hemorrhage | 3 | 4.05 |
| Pulmonary edema | 1 | 1.35 |
| Cardiac Dilatation | 1 | 1.35 |
| Fibrillation | 1 | 1.35 |

Total number of cases with early complications, 20

TABLE X
LATE COMPLICATIONS OF OPERATION

| | NUMBER OF PATIENTS | PERCENTAGE |
|------------------------|--------------------|------------|
| Obstruction | 8 | 10.80 |
| Abscess | 3 | 4.05 |
| Superficial infection | 2 | 2.70 |
| Duodenal fistula | 2 | 2.70 |
| Embolism | 2 | 2.70 |
| Evisceration | 2 | 2.70 |
| Superficial separation | 2 | 2.70 |
| Hypostatic pneumonia | 1 | 1.35 |

Total number of cases showing late complications, 18.

early complications are by far the more serious, for all the deaths occurred in patients whose complications developed immediately after operation; those whose complications developed later in the postoperative period were all able to weather the storm. The most frequent complication was atelectasis which occurred in thirteen of our patients (17.5 per cent), with no fatalities. This condition is just as common after spinal as after general anesthesia. Ileus developed in twelve patients (16.2 per cent), all of whom recovered. The use of spinal anesthesia has decidedly reduced the frequency of this complication. Shock appeared in seven patients, 9.5 per cent of the series, but since we have adopted routine intravenous glucose and blood transfusions during the course of the operation, we have had not a single case of shock.

Leakage of bile from the insecurely closed duodenal stump or from injury to the common bile duct was the most serious of all complications because of the development of bile peritonitis from obstruction and perforation of the jejunum proximal to the gastrojejunal anastomotic site. There were two more patients who developed duodenal fistula as a late complication, but they both recovered.

TABLE VIII
PATHOLOGIC DIAGNOSIS

| | NUMBER OF CASES | PERCENTAGE |
|-------------------------------|-----------------|------------|
| Gastric ulcer | 18 | 24.4 |
| Gastric ulcer with gastritis | 4 | 5.4 |
| Total | 22 | 29.8 |
| Duodenal ulcer | 32 | 43.3 |
| Duodenal ulcer with gastritis | 15 | 20.3 |
| Total | 47 | 63.0 |
| Carcinoma | 5 | 6.6 |
| Total | 74 | 100.0 |

fornity than is gastric ulcer. On the other hand, a gastric ulcer definitely is potentially more dangerous to life than a duodenal ulcer because of the tendency to malignant degeneration. In our small series, five, or 18.5 per cent, of the twenty-seven gastric ulcers showed malignant changes on microscopic examination. On the basis of these findings alone, the importance of recommending operation for all patients with intractable gastric ulcers must be obvious. It can be reasonably anticipated that the probability of cure by operation for gastric carcinoma in the subclinical stage must be excellent when compared with the very discouraging results obtained by gastric resection in the usual patients with stomach cancer who come to the surgeon. Worthy of comment also is the number of cases of gastritis, especially in association with duodenal ulcer, which in our series approximated 50 per cent. Undoubtedly, the well-being of the patient after partial gastrectomy may be attributed, in part at least, to removal of diseased gastric mucosa. It is not alone freedom from annoying pain, but also relief from chronic dyspepsia, that enables many of these semi-invalids to resume their normal activities after operation. This point, so well stressed by European observers, is so infrequently disensed in this country that some authors, attempting to discredit partial gastrectomies for ulcer, have suggested that peptic ulcer is not a comparable condition on the two continents.

Postoperative Complications.—The number of postoperative complications has steadily decreased with increased experience in the management of these cases. The use of the nasal catheter with constant suction has removed all anxiety regarding leakage at the anastomotic stoma. When the amount of drainage removed from the stomach is measured, the relief of tension in the suture line can be readily appreciated. In our experience, the employment of the indwelling stomach tube has been the greatest single factor in reducing the mortality and morbidity of gastric surgery. It is our practice to leave the tube in the stomach for five days. This allows patients to swallow frequently small amounts of water for which they are very grateful, and at the same time it pre-

TABLE XII
END RESULTS

| | NUMBER OF CASES | PERCENTAGE |
|----------------|-----------------|------------|
| Excellent | 34 | 48.6 |
| Good | 21 | 30.0 |
| Fair | 6 | 4.2 |
| Poor | 3 | 8.6 |
| Not classified | 6 | 8.6 |
| Died | 4 | |
| Total | 74 | 100.0 |

slight restriction in diet. A single complaint such as occasional distress or the necessity for frequent meals was enough to place an otherwise excellent result into the "good" classification. "Fair" indicates that the patient was improved over his preoperative condition but still had some complaints, enough to consider the operation not entirely satisfactory. "Poor" means practically no improvement.

SUMMARY

1. A report is presented of seventy-four consecutive partial gastrectomies for peptic ulcer performed at the Henry Ford Hospital during the five-year period, 1934 to 1939 inclusive.

2. The mortality for this group was 5.3 per cent, and all deaths were due to peritonitis. There has not been a fatality among the last thirty-four patients in the series.

3. The males outnumbered females nine to one.

4. Over one-half of the patients had submitted to previous operations on the gastrointestinal tract.

5. Pain, nausea, and vomiting were the most constant symptoms of ulcer, being present in 85.2 per cent and 70.2 per cent of the patients, respectively.

6. Roentgenograms were the greatest single aid to diagnosis. Positive findings corroborated at operation were recorded in over 90 per cent of the cases.

7. The ratio of duodenal to gastric ulcer was two to one, whereas the ratio in our perforated ulcer series¹⁰ was three to one.

8. One patient of the four who died, died after the development of early postoperative complications; all survived late complications.

9. The end result was excellent or good in 75 per cent of the patients.

10. Carcinoma, which was suspected neither clinically nor by the surgeon at operation, was diagnosed by the pathologist in five patients with gastric ulcer.

CONCLUSIONS

Partial gastrectomy yields such satisfactory results in the treatment of selected cases of peptic ulcer which do not respond to medical management that it is firmly established as the operative procedure of choice.

Cause of Death.—All four deaths in this series were caused by peritonitis. Bile peritonitis occurred in three instances, twice from a leaking duodenal stump and once from injury to the common bile duct. The remaining death resulted from kinking obstruction and eventual perforation of the jejunum proximal to the gastrojejunal anastomotic site. It is instructive to note that three of the four deaths occurred in patients operated upon because of intractable hemorrhages, and that, in all but one patient, the factor determining the fatal issue was technical difficulty in closing the duodenal stump, because the ulcer had penetrated into the head of the pancreas. These findings indicate that Finsterer's suggestion of sectioning the stomach proximal to the pylorus in difficult cases might be adopted with profit.

TABLE XI
FOLLOW-UP

| | NUMBER OF CASES | PERCENTAGE |
|-----------------|-----------------|------------|
| Less than 6 mo. | 22 | 31.4 |
| 6 mo. to 1 yr. | 11 | 15.7 |
| 1 yr. to 2 yr. | 11 | 15.7 |
| 2 yr. to 5 yr. | 26 | 37.2 |
| Died | 4 | |
| Total | 74 | 100.0 |

Results of Operations.—Some idea of the end results of partial gastrectomy may be obtained from a study of Table XI. Our follow-up has been relatively effective, for approximately one-half of the patients in the series were followed for more than one year subsequent to operation, and one-third of them for from two to five years. Actually, there were very few untraced patients, for one-half of those in the group of 31.4 per cent who were followed less than six months were operated on so recently that they fell into the classification.

The average period of restricted activity after leaving the hospital was only 1.3 months. Less than one-half of these patients, despite advice, remained on a restricted diet after six months. The diets of the remainder were only moderately restricted. Marginal ulcer, proved by x-ray, developed in three patients, and in an equal number it was suspected, but this sequela occurred only in those patients in whom limited resection had been performed. Over 40 per cent gained greatly in weight, and practically all the rest gained slightly. Including the patients with suspected and proved marginal ulcer, 10.8 per cent still have some gastric distress, but in most instances this is only slight and readily controlled by alkaline or food.

A detailed classification of the end results is tabulated in Table XII. There it is shown that approximately 75 per cent of the patients had good or excellent results.

A patient was classified as having an excellent result if he was satisfied and if he had no complaints, no restriction of activity, and only

TRANSPLEURAL ESOPHAGOGASTROSTOMY FOR CARCINOMA OF THE ESOPHAGUS AND FOR CARCINOMA OF THE CARDIAC PORTION OF THE STOMACH

A REPORT OF TWO CASES

B. N. CARTER, M.D., JEAN STEVENSON, M.D., AND
OSLER A. ABBOTT, M.D., CINCINNATI, OHIO

*(From the Department of Surgery, College of Medicine of the University of
Cincinnati, and the Cincinnati General Hospital)*

IN THE instances in which it can be accomplished, the resection of the lower end of the esophagus, of a portion of the cardiac end of the stomach, or of portions of both followed by esophagogastrostomy offers the most satisfactory method of dealing with carcinoma in these areas. By this procedure the growth can be extirpated and the continuity of the stomach and esophagus restored in one stage, thus avoiding the necessity for the formation of antethoracic skin tubes or for the use of rubber tubes to allow the act of swallowing to be completed. This operation should have a wide field of usefulness in view of the fact that from 33 to 50 per cent of all carcinomas of the esophagus are said to occur in the lower one-third of this organ and about 10 per cent of all those in the stomach occur at the cardia.

The approach to lesions in the cardiac end of the stomach and in the lower end of the esophagus is easier when carried out through the chest than when attempted through the abdomen. After a preliminary artificial pneumothorax has been induced, the thorax can be safely opened through an intercostal incision in the seventh or eighth interspace and an excellent exposure of the terminal third of the esophagus and diaphragm can be had (Fig. 3). When the diaphragm had been widely opened from the esophageal hiatus to the costal margin, an easy access is afforded to the entire stomach, spleen, and a portion of the liver (Fig. 4). The stomach can be readily mobilized, as can the lower half of the esophagus; and, after portions of them have been resected, the anastomosis can be completed under direct vision without having to work down in a small, dark wound (Fig. 7). If the wound edges are protected, and the pleural cavity packed off with sponges, there is little danger of empyema due to soiling the pleural cavity. Empyema follows leakage at the line of anastomosis rather than soiling at the time of operation.

The feasibility and desirability of the operation of esophagogastrostomy have long been recognized. This is evidenced by the reports in the literature dealing with the subject of esophagogastrostomy. As far back as 1895, Biondi¹ was attempting this operation on dogs. The first

The already low mortality rate is steadily decreasing. We attribute our decrease in the mortality rate to improved operative technique resulting from increased experience and to the adoption of such measures as the use of spinal anesthetics, routine blood transfusions during operation, continuous gastric suction in the postoperative period, and administration of oxygen both during and immediately after the operation to avoid anoxia and to lessen the occurrence of pulmonary complications.

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remove any pull or drag on the point of anastomosis; and second, by stitching the diaphragm well down on the stomach, rather than close to the line of suture between the stomach and the esophagus. Recently in some experimental work we have anchored both the stomach and the esophagus to the chest wall (periosteum of the rib or of a vertebral body) so that the line of anastomosis between the stomach and the esophagus can actually be displaced from side to side and from above down without the least pull on it (Fig. 1). We believe that this is a most important point in the technique and that by utilizing it one can completely avoid tension.

TABLE I

SUCCESSFUL ESOPHAGOGASTROSTOMIES REPORTED IN THE LITERATURE

| SURGEON | NUMBER OF CASES | YEAR | OPERATION | PERIOD OF SURVIVAL | CAUSE OF DEATH |
|-----------------------------------|-----------------|--------------|---|------------------------------|----------------------|
| Voelcker ³ | 1 | 1907 | Resection of carcinoma of cardiac portion of stomach through abdominal approach | "Months" | Metastasis |
| Kümmel ⁷ | 2 | 1909 1910 | Resection of carcinoma of cardiac portion of stomach through abdominal approach | "Months" | Metastasis |
| Bircher ⁸ | 1 | 1918 | Carcinoma of cardia and lower esophagus through transabdominal approach | 18 mo. | Metastasis |
| Gohrbandt ⁹ | 1 | 1921 | Carcinoma of esophagus just above cardia; abdominal approach | 6 mo. | Intercurrent disease |
| Ohsawa ¹⁰ | 8 | 1934 | Carcinoma of the lower one-third of esophagus; transthoracic approach | No statistics given | No statistics given |
| Marshall ⁶ | 1 | 1938 | Carcinoma of terminal esophagus; transthoracic approach | Since 1938 | |
| Adams and Phemister ⁵ | 1 | 1938 | Carcinoma of terminal esophagus; transthoracic approach | Since 1938 | |
| Cattell ¹¹ | 1 | 1939 | Carcinoma lower esophagus and stomach; two-stage combined abdominal and transpleural approach | Living 5 mo. after operation | |
| Garlock ¹³ | 1 | 1939 | Carcinoma of lower end of esophagus; transpleural approach | Living 9 mo. after operation | |
| Ochsner and DeBakey ¹² | 1 | 1939 | Carcinoma of lower end of esophagus; transpleural approach | Living | |

The rent in the diaphragm through which the stomach has been brought into the thorax must be partially closed and the edges of the diaphragm then sutured to the stomach in order to prevent herniation of the intestine through the diaphragm. When the diaphragm is sewed to the stomach, care must be taken to attach it well down toward the

surgeon to perform the operation on a human being was Wendel,² who, in 1907, resected a carcinoma of the cardia and esophagus and, having closed both organs, did a lateral anastomosis between them with a modified Murphy button. His patient died in twenty-four hours of hemorrhage. In 1908 Voelker³ performed the first successful esophagogastrostomy on a human being after having removed a carcinoma of the cardiac end of the stomach through a transabdominal route. Good summaries of the literature can be found in articles by Bird⁴ in 1939 and by Adams and Phemister⁵ in 1938. The varied techniques and the ingenious schemes for performing satisfactory anastomosis of the esophagus and stomach bear witness to the fact that until very recent years no one operation as performed on human beings had been found which was satisfactory enough to recommend itself to the surgical profession. The successful case reported by Adams and Phemister⁵ in 1938 after numerous laboratory experiments and the case of Marshall⁶ likewise reported in 1938 have given considerable hope that now the operation is on a firmer basis than ever before. As shown in Table I, only eighteen successful esophagogastrostomies have been reported. The cases reported here bring the total number to date to twenty.

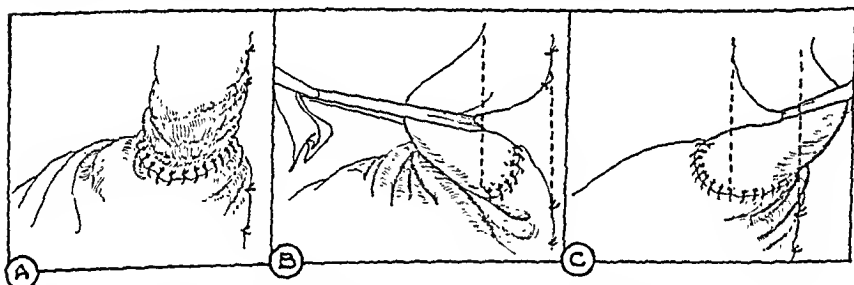


Fig. 1.—A, The stomach and esophagus have been sutured to the periosteum of nearby ribs so as to relieve tension on the suture line. Note the folds in esophagus and stomach indicating relaxation. B and C, With tension relieved, the anastomosed viscera can be displaced from side to side without any pull on the suture line.

The majority of the failures of the methods which have been used in the past have been due to two causes; viz., shock and leakage at the suture line. With the improved technique of operating, with better methods of anesthesia, with the recognition of the importance of pre-operative pneumothorax, and with the increased use of blood transfusions, the danger from shock has practically disappeared and can now be placed at a minimum. The most potent cause for leakage at the suture line has been tension on the line of anastomosis. One has only to read the literature to be convinced of this. In the laboratory one can control leakage at will by the degree of tension on the line of suture. To ensure an intact suture line, tension must be avoided. We have attempted to obviate tension in two ways: first, by anchoring the stomach to the periosteum of a nearby rib in such a way as to

When the two patients, whose case histories are being reported, were operated upon, we had not done any experimental work on the suturing of the stomach and esophagus, but we were familiar with most of the literature dealing with esophagogastrostomy. The method in which the end of the esophagus was introduced into the stomach through a slit in its anterior wall and the stomach then pulled up around it with inverting sutures appealed to us as a method of choice. This is the method which has been advocated by Bircher,⁸ Meyer,¹⁴ Fischer,¹⁵ and Bengolea¹⁷ and is the method which was used in both of our cases (Fig. 2). Although there was no leakage in either instance, there were strictures in each and both patients have had to have repeated dilatations in order to be able to swallow. We felt that in Case 1 the stricture probably resulted from not having placed enough esophagus into the stomach.

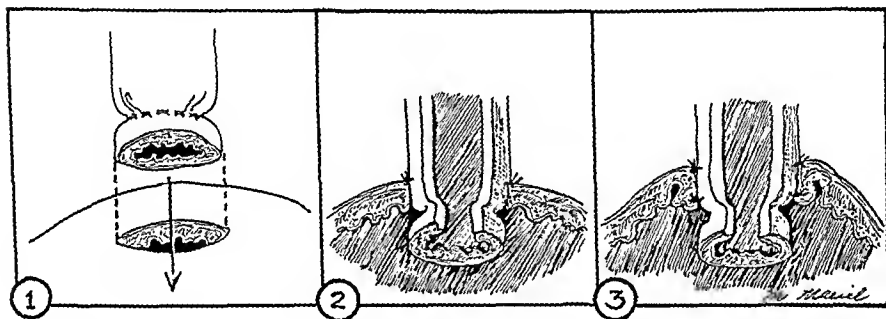


Fig. 2.—The type of anastomosis which was performed in the two reported cases. The end of the esophagus was introduced into the stomach and inverted into the latter with two rows of Lembert sutures of silk.

In Case 2, therefore, at least one inch of esophagus was introduced through the incision in the anterior wall of the stomach, nevertheless, a stricture resulted. Following our experience with strictures in these two cases, we have performed a series of experiments on animals in the laboratory and have come to feel that the above-described type of anastomosis is not desirable. It uses up an unnecessary length of esophagus; it is apt to cause early obstruction to the lumen of the esophagus by the latter's inverting into itself and to cause late strictures due to the fact that the end of the esophagus which projects into the stomach does not slough away but heals together forming a diaphragm-like stricture. The details of this experimental work will be published in a later communication.

CASE 1.—(Cincinnati General Hospital, No. 103557.) K. B., a white woman, aged 54 years, was admitted to the Cincinnati General Hospital on Sept. 15, 1938, complaining of vomiting and loss of weight. Five months before admission she had noted a slight difficulty in swallowing while she was eating a fried egg. The dysphagia had increased in severity until for the past four weeks she had been unable to swallow liquids and she had vomited everything which she attempted to swallow. She had never vomited blood. There had been a loss of twenty-four pounds in weight in the past six weeks. She had never had pain on swallowing.

greater curvature so as to place plenty of stomach in the thorax. The tendency is to stitch it too close to the anastomosis and thus create a drag on it.

In the two cases reported here, the stomach was securely anchored to the periosteum of a nearby rib, after the anastomosis had been finished, with four sutures of silk. If the stomach is lifted high enough into the thorax so that there is no tension on the anastomosis and then held at that point by stitching it to the chest wall, the danger of drag on the line of anastomosis is decreased. In one of the cases mentioned in this report, it was necessary to reopen the thorax one month after the original operation. At that time the stomach was found to be firmly adherent to the chest wall and there was no tension on the line of anastomosis. As will be seen in the following case reports, the end-to-side anastomoses between stomach and esophagus were not done aseptically, but, since there was no leakage at the suture line, the pleura was able to cope with the small amount of soiling and no empyema resulted in either case. In both instances the wound in the chest wall healed per primam.

Gastrostomy had been done in each instance weeks or months before the actual anastomosis between stomach and esophagus was performed. In spite of this the stomach could be mobilized well enough to allow a sufficient portion of it to be pulled up into the chest to reach the esophagus without tension. It would make the operation much simpler if a gastrostomy were not done as a preliminary. A jejunostomy would serve the same purpose and not interfere with the mobilization of the stomach. Though the operations were time consuming, the patients did not suffer from shock and at no time were their conditions alarming. In each instance transfusions of citrated blood were given during the operation.

Dragstedt¹⁶ has shown the frequent occurrence of pneumonia in dogs following obstruction to the esophagus. The saliva overflows from the obstructed esophagus and is aspirated into the bronchial tree and thus gives rise to pneumonia. It also occurred to us that, if peristalsis was kept at a minimum in the esophagus for several days after the esophago-gastrostomy was performed, there would be less danger of leakage at the suture line. For these two reasons the esophagus was kept empty after operation by continuous suction applied to a catheter placed in the esophagus. It was surprising how much saliva was evacuated from the esophagus in twenty-four hours. We believe that continuous suction in the esophagus after operation is of definite value. The patients were not allowed to attempt to swallow fluids until ten days after operation. The induction of a preliminary artificial pneumothorax was attempted in each case. In one it was complete, in the other only partial, due to the presence of many filmy adhesions. In each case the operation was carried out under local anesthesia down to the pleura and thereafter cyclopropane was used.

Physical examination showed a thin, pale, woman who appeared to be 64 years of age, rather than her given age of 54 years. She showed evidence of marked loss of weight and was highly nervous and apprehensive. The skin was dry and wrinkled. Except for a few enlarged glands in the groins, there was no adenopathy. Her lungs were clear. The heart sounds were clear. No masses could be made out in the abdomen.

X-ray examination after ingestion of barium showed a dilatation of the esophagus down to the cardiac end of the stomach, where a smooth-walled point of obstruction was seen. The Wassermann reaction was negative. Esophagoscopy revealed a cauliflower-like growth at the junction of esophagus and stomach which was projecting into the lumen of the esophagus and involving the terminal 2 cm. of the esophagus. A biopsy from the growth showed it to be an adenocarcinoma of the stomach with considerable mitosis in many of the cells.

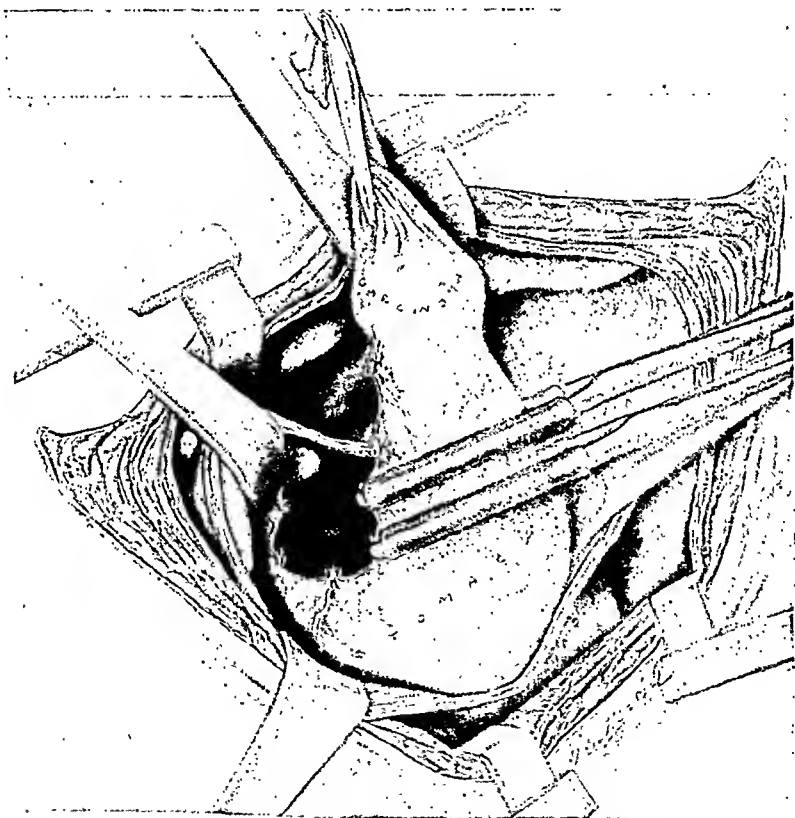


Fig. 5.—Case 1. The stomach has been freed more by dividing some of the vessels along the greater curvature and clamps have been applied beyond the growth.

On Oct. 1 a Janeway gastrostomy was done under local anesthesia. At this time a mass about 6 cm. in diameter was felt at the cardiac end of the stomach, a small gland was felt along the lesser curvature of the stomach, and the liver was found to be free of metastatic nodules. The gastrostomy functioned well and the patient gained six pounds in the first four weeks after operation. She was given a blood transfusion of 325 c.c. of citrated blood on Nov. 3 and another of 575 c.c. on Nov. 4. An attempt at the production of an artificial pneumothorax was unsuccessful owing to the presence of many adhesions between the lung and the pleura.

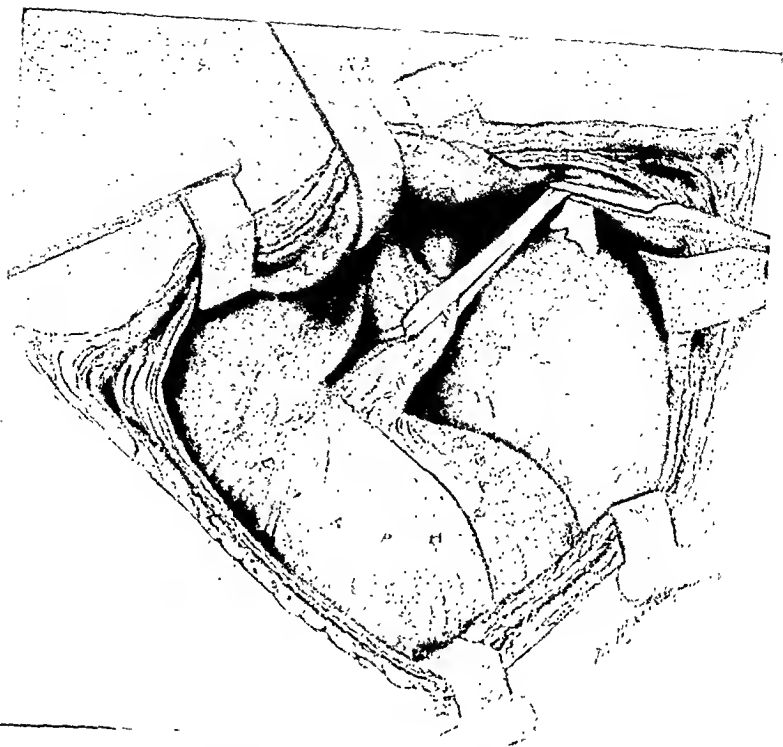


Fig. 3.—Case 1. The exposure after lung has been retracted. The esophagus has been freed and a tape passed around it.

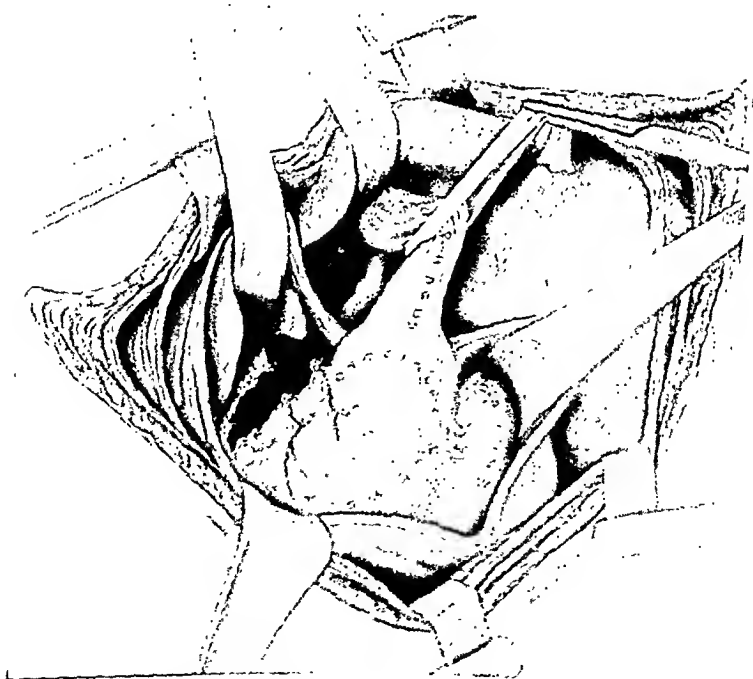


Fig. 4.—Case 1. The diaphragm has been split, the lesser curvature partially divided, and the stomach drawn up into the thorax.

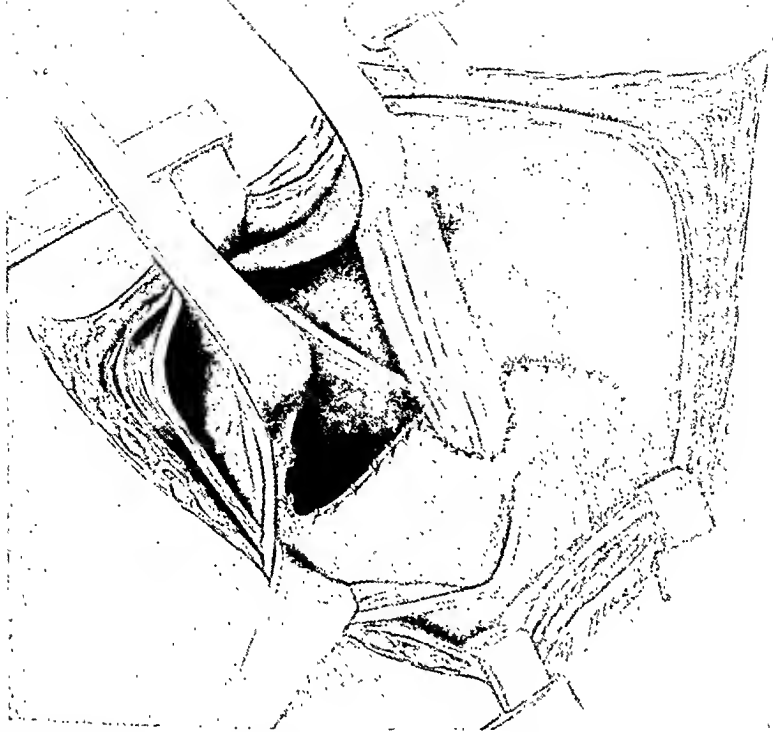


Fig. 7.—Case 1. The end of the esophagus has been introduced into the stomach through a slit and has been inverted into the stomach with two rows of Lembert sutures of silk.

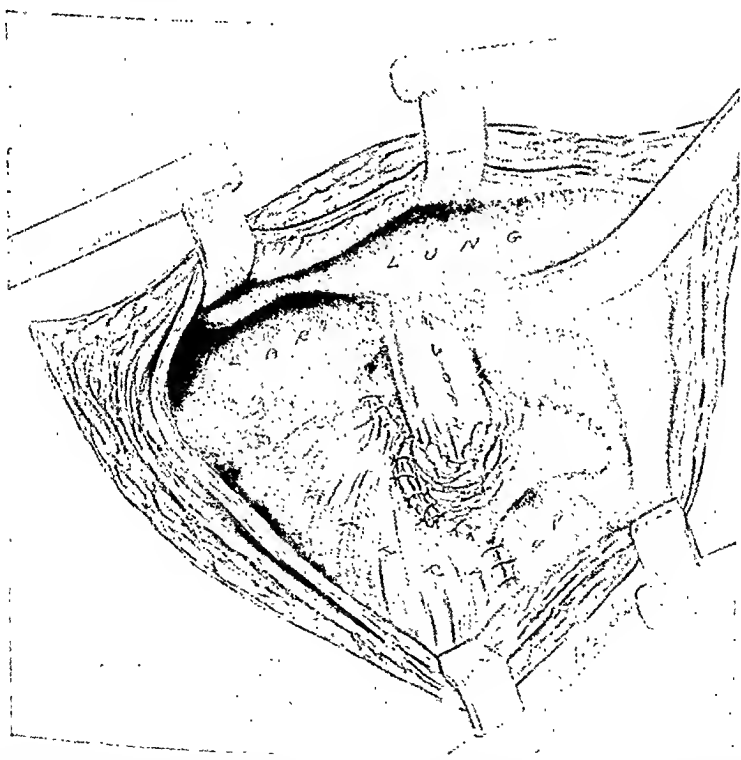


Fig. 8.—Case 1. A piece of omentum has been placed over the suture line, the diaphragm partially closed with silk, and the remainder sutured to the stomach with interrupted silk sutures.

Under local and cyclopropane anesthesia she was operated upon on Nov. 8, 1938. A long curved incision was made down to the pleura in the seventh interspace from the midaxillary line to the midscapular line, where it was curved upward to the fourth rib. One inch of the vertebral ends of ribs VII, VI, V were resected, the pleura opened throughout the extent of the incision, and the chest spread widely open. Filmy adhesions were found binding the whole left lung to the pleura. The lower lobe of the lung was completely freed and retracted and the left phrenic nerve was crushed. The lower three inches of the esophagus were freed by sharp and blunt dissection and tapes were placed about the freed esophagus (Fig. 3). The diaphragm was now split in the direction of its fibers from the hiatus to the costal edge and the cardiac end of the stomach and esophagus dissected free. The stomach could now be partially delivered into the thorax and an excellent exposure of the stomach and lower esophagus was had. A tumor mass 5 cm. in diameter was found occupying the cardiac end of the stomach and extending into the terminal 2 cm. of the esophagus. There was one small hard gland on the lesser curvature close to the cardia,

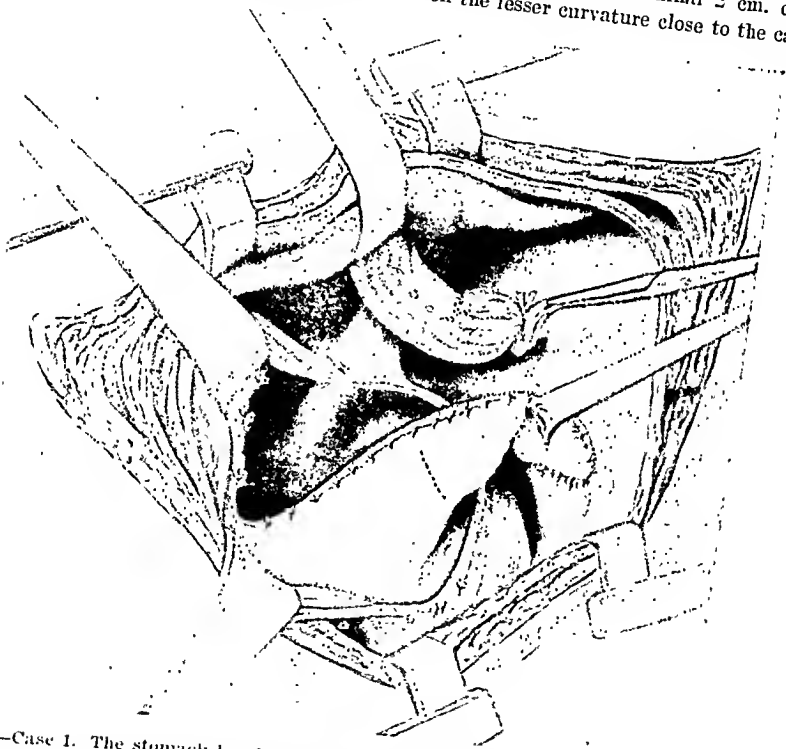


Fig. 6.—Case 1. The stomach has been closed and the growth resected. The esophagus has been closed with a purse-string suture of No. 00 plain catgut. The dotted line indicates the line of incision in the stomach (it has been made in this direction to preserve blood supply). The stomach has been anchored to the peritoneum of the seventh rib.

but the liver showed no evidence of metastases. The lesser curvature was freed by dividing the left gastric artery about midway down the curvature. This allowed much more stomach to be pulled into the thorax (Fig. 4). The vessels along the greater curvature were divided between trans-fixion suture of silk from the esophagus down to the middle of the greater curvature.

Payr clamps were placed across the stomach well below the lower margin of the tumor and the stomach divided between the clamps (Fig. 5). The Payr clamp was

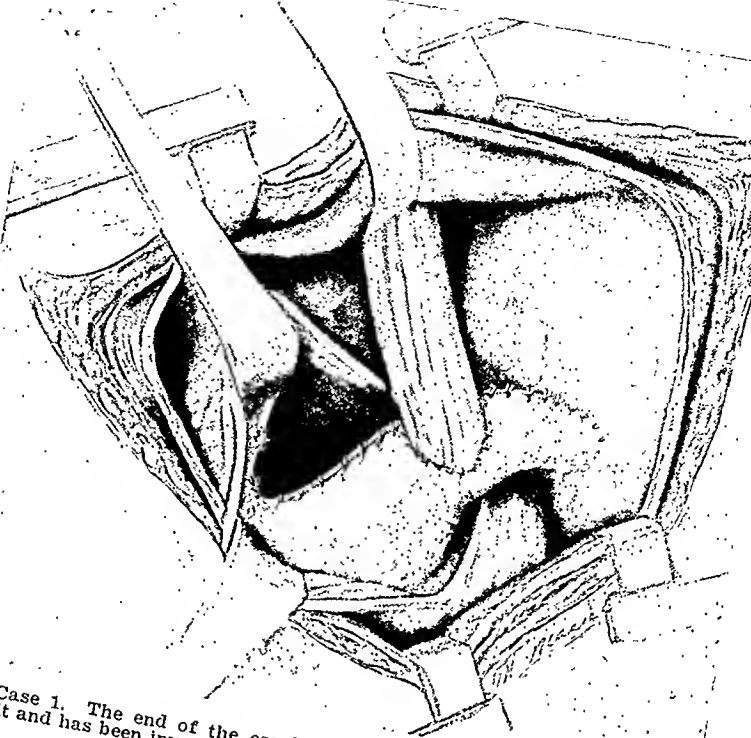


Fig. 7.—Case 1. The end of the esophagus has been introduced into the stomach through a slit and has been inverted into the stomach with two rows of Lembert sutures of silk.

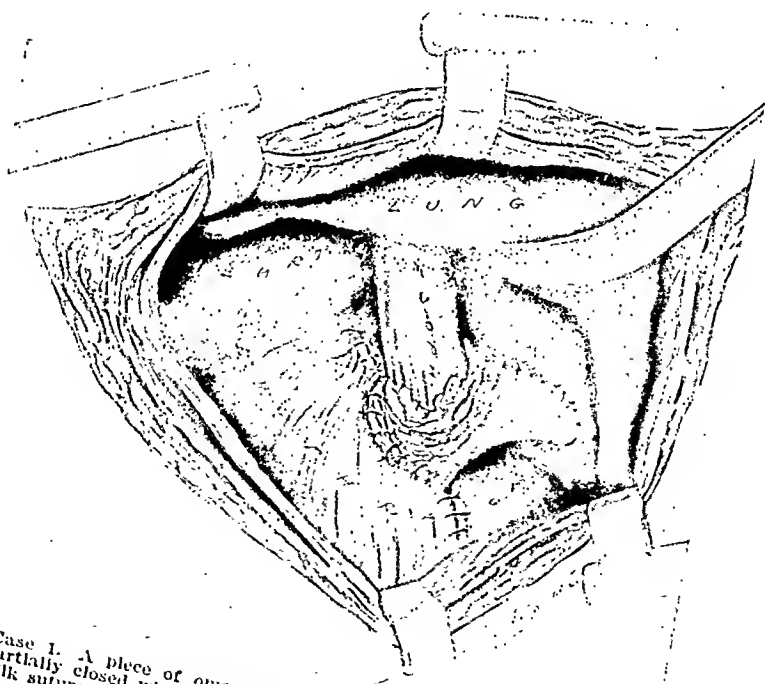


Fig. 8.—Case 1. A piece of omentum has been placed over the suture line, the diaphragm partially closed with silk, and the remainder sutured to the stomach with interrupted silk sutures.

removed and the stomach closed with a continuous through-and-through lock stitch of No. 1 chromic catgut. This line of suture was now inverted beneath a row of Halsted mattress sutures of medium silk. This left a tube of stomach which could be easily delivered into the thorax, where it was anchored to the periosteum of a rib close to the spine and with four sutures of medium silk (Fig. 6).

A purse-string suture of No. 0 plain catgut was now placed around the esophagus well above the tumor and the esophagus divided between it and a Kocher clamp. An incision 2 cm. long was made in the tube of stomach at right angles to the long axis of the stomach tube (Fig. 6). It was felt that an incision made in this direction would not interfere as much with the blood supply to the tube as would one parallel to the curvature. The lower end of the esophagus, still closed with the purse-string suture, was introduced into the stomach through this incision and the stomach united to the wall of the esophagus with two rows of Halsted mattress sutures of silk (Fig. 7). A piece of omentum was brought up and sutured over the line of anastomosis. The rent in the diaphragm was closed up to the tube of stomach with interrupted sutures of silk and the diaphragm stitched to the tube with sutures of the same material (Fig. 8). The pleural cavity was now thoroughly irrigated with a large amount of normal salt solution. Two mushroom catheters were inserted into the eighth interspace, one in the anterior axillary and one in the pleural cavity in the eighth interspace. The ribs were pulled together with three pericostal sutures of kangaroo tendon and the muscles closed in layers with continuous suture of No. 1 chromic catgut. The skin was closed with interrupted silk with no drainage of the wound itself. The lung was completely expanded prior to the closure of the chest wall.

A transfusion of 900 c.c. of blood was given during the operation, which lasted for three hours. The operation was well tolerated, the patient's blood pressure being 100, pulse 114, and respirations 30 at the close of the operation.

After operation a nasal tube was introduced well down into the esophagus and continuous suction was maintained for ten days. At the end of that time the patient was unable to swallow liquids and continued unable to do so. X-ray and esophagoscopy examination showed the presence of a stricture at the site of anastomosis and this was unable to be penetrated either from above or from the gastrostomy below. A cystoscope was repeatedly introduced by Dr. Henry Freiberg into the stomach through the gastrostomy and the cardia visualized, but no opening could be seen or entered. It was evident that the stricture must be dealt with surgically.

On Jan. 4, 1939, two months after the first operation, the wound was reopened under local anesthesia and the anastomosis inspected. There were few adhesions about it, no evidence of recurrence and from the outside it looked perfect. However, one was unable to feel any lumen at the point of anastomosis, but only hard dense scar within the lumen of the esophagus. A metal sound was introduced through the gastrostomy opening and after considerable difficulty was pushed through the stricture into the esophagus under direct guidance. The condition of the patient was such that further maneuvers were abandoned and the wound closed. After this operation nothing passed through the stricture and attempts at swallowing a string were futile.

On Jan. 7, 1939, the wound was again reopened under local anesthesia and the anastomosis inspected. There was no change in its appearance. A longitudinal incision from above downward was made through the stricture, partly in the esophagus and partly in the stomach. The stricture was composed of very dense fibrous tissue, but no recurrence of the carcinoma could be seen. A ureteral catheter was introduced into the opening in the esophagus, and pushed out of the mouth. A braided silk thread was attached to this and it was pulled down through the opening in the esophagus. A sound was passed up from the gastrostomy into the incision through the stricture, the braided silk thread attached to it and this thread pulled out through the gastrostomy opening. The braided silk string was thus pulled

through the stricture and was left in place. The incision through the stricture was now closed transversely to the long axis of esophagus and the chest closed as before.

Following this operation, dilators of increasing size were threaded on the braided silk cord and pulled through the stricture from below upwards. After a few weeks a No. 36 French dilator could be easily pulled through the stricture. The patient was then able to swallow liquids, soft foods, and small pieces of hard food. She gained ten pounds in weight. However, in spite of the fact that large-sized dilators would pass through the stricture from below upwards, the patient had periods in which swallowing was very difficult and she would occasionally vomit.

In August, 1939 (nine months after operation), she was readmitted to the Cincinnati General Hospital complaining of difficulty in swallowing, pain in the lumbar region and pain in the stomach when feedings were introduced through the gastrostomy. The cardiac end of the stomach was inspected through a cystoscope introduced through the gastrostomy and no evidence of recurrence seen. An esophagoscope was passed and a small slitlike opening seen with scar tissue piled up around it, but no recurrence was made out. X-ray examination failed to show metastases to the spine or ribs. She was fed through the gastrostomy and seemed to improve slowly for three weeks. On Aug. 21, 1939, she died suddenly.

An autopsy was performed, but no cause for death was found. No recurrences were discovered and there was no evidence of metastasis. The suture line was intact. The esophagus was dilated just above the stricture into a small sac-like segment. The stricture was nearly complete, only a tiny slitlike opening remaining. The walls of the stricture were composed of extremely hard, dense fibrous tissue. No carcinoma was present in the stricture.

Comment.—A jejunostomy rather than a Janeway gastrostomy should have been done in this case when it was found that the growth was in the cardiac end of the stomach and the lower end of the esophagus. The delivery of the stomach into the chest was certainly hindered by the gastrostomy, but even with the gastrostomy enough stomach could be pulled up to permit a satisfactory esophagogastrostomy to be done.

It was felt that there were two reasons for the occurrence of the stricture: first, that not enough esophagus was introduced into the opening in the stomach so that, when contraction during healing occurred, the short stump of esophagus pulled out of the stomach and the edges of the esophagus healed together, thus accounting for the stricture; second, that the opening in the stomach was made at right angles to the axis of the stomach, rather than parallel to it, so that when the stomach musculature contracted it tended to close the opening rather than widen it.

Apparently the cancer had been completely removed since no recurrence or metastasis was found at autopsy. If the stoma had functioned properly, the patient would have been well and probably free from her cancer for the rest of her life.

No cause was found at autopsy for this patient's death, but it must have been dependent in some way upon her stricture with consequent inanition.

An excellent exposure of the entire stomach or lower esophagus was obtained through the transpleural approach, and the anastomosis was performed more easily than it could have been by abdominal approach.

CASE 2.—Mrs. M. P. (Christian R. Holmes Hospital No. 390448), aged 58 years, was admitted to the hospital on May 8, 1939. Her present illness had begun in May, 1938, at which time she first experienced difficulty in swallowing. Within a few weeks she was unable to swallow solid foods and regurgitation after swallowing was common. In July, 1938, she was referred to a roentgenologist, who found almost a complete obstruction at the lower end of the esophagus. For two months she remained on a liquid diet and lost from twenty-five to thirty pounds in weight.

In September, 1938, an esophagoscopy was done. A constricting, ulcerative lesion was found in the lower one-third of the esophagus and a biopsy was taken. The pathologist's report was "squamous-cell carcinoma." The constriction was dilated every three or four days for several weeks to permit saliva to pass, but the esophagus would close again in a very short time. Because of her rapid loss of weight and strength, a gastrostomy was performed on Oct. 5, 1938. This procedure checked further loss of weight, but did not relieve the regurgitation of saliva.

The patient related that for two years preceding the difficulty in swallowing she had been troubled with indigestion, belching, and an occasional epigastric pain which radiated straight through to the back. When the difficulty in swallowing developed, she experienced the sensation of a lump behind her heart which could be relieved only by vomiting. She did not vomit blood and there were no black or tarry stools.

With the complete obstruction of the esophagus, constipation became so severe that she required frequent laxatives. Stagnation and fermentation of the saliva in the esophagus was one of her worst complaints and was a source of great embarrassment. She learned to regurgitate this material almost at will so that she could empty the esophagus before appearing in public. However, she could not escape the odor and taste of the fermented saliva and mucus. These alone, and not the desire to take food by mouth, were responsible for her seeking surgical aid.

The patient was an emaciated woman, very active and mentally clear. She weighed sixty-four pounds. The skin was loose and dry. The mucous membranes had good color. Other than a foul halitosis, a gastrostomy through the upper left rectus muscle, and signs of malnutrition, the examination was not remarkable.

On fluoroscopic examination a complete obstruction was demonstrated in the lower esophagus about 7 cm. from the cardia. The esophagus was greatly dilated above the obstruction and exhibited powerful peristaltic action. Barium introduced through the gastrostomy showed the fundus of the stomach to be normal. Roentgenograms of the chest and spine showed no evidence of metastases. Artificial pneumothorax was begun on the left on May 9, 1939, and after four treatments a complete collapse of the lung was effected. The esophagus was irrigated thoroughly several times a day. The patient's oral hygiene was good and with adequate care of the esophagus the halitosis and objectionable taste in the mouth largely disappeared.

Two weeks after her first pneumothorax treatment the patient was operated upon. The operation was begun under local anesthesia. An incision was made along the course of the seventh interspace up to a point two and one-half inches from the spine, where it was curved upward to the fifth rib. The incision was deepened down to the pleura and a one-inch segment of the seventh rib was resected close to the spine. Hemostasis was secured with electrocoagulation, after which the operation was continued under cyclopropane anesthesia. The pleura was opened and the chest spread widely with rib spreaders. The wound edges were carefully protected with moist towels. The lung was found to be well collapsed and free of adhesions. The terminal esophagus and aorta were easily visualized. The phrenic nerve was isolated just above the diaphragm and crushed. The loose parietal pleura over the esophagus was incised in a linear direction and continued upward into the inferior pulmonary ligament.

A tumor could be felt in the esophagus, but apparently there was no spread to the pleura or mediastinal glands. The esophagus was constricted by a dense annular growth rather than enlarged by a space-consuming mass. The tumor mass measured two inches in length and was located one and one-half inches above the diaphragm (Fig. 9). Sections later showed the lumen to have been completely obliterated. By blunt dissection, the esophagus was easily freed from the diaphragm to the arch of the aorta. In attempting to keep as much of the areolar tissue as possible with the esophagus, the right pleura was wiped too close and a small leak later developed which made it necessary to complete the operation under positive pressure anesthesia.

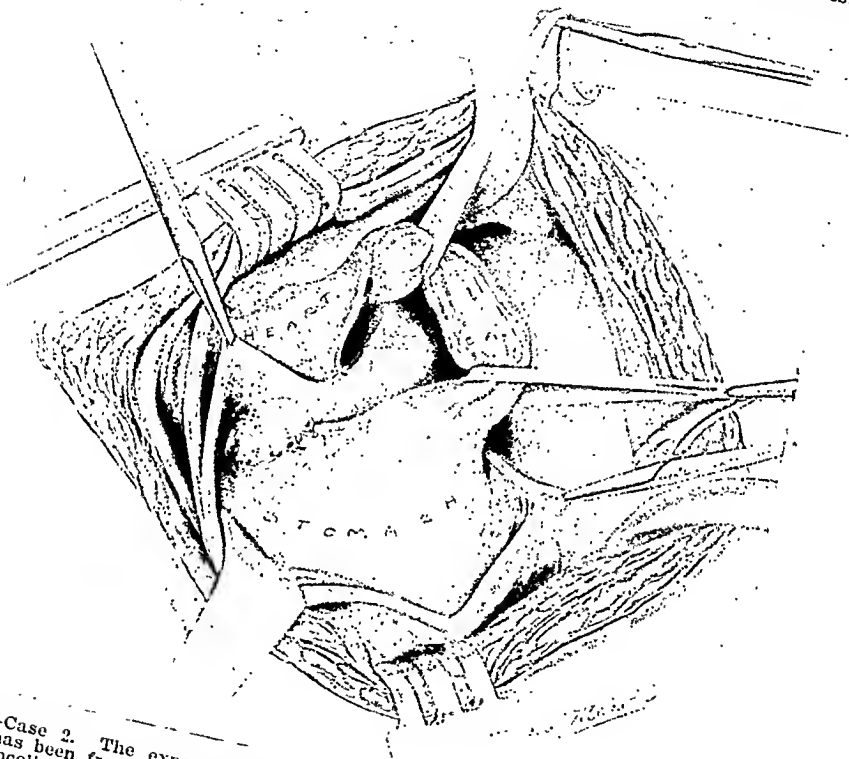


Fig. 9.—Case 2. The exposure of the carcinoma in the lower esophagus. The esophagus has been freed nearly to the aortic arch, the diaphragm opened, and part of the gastrocolic omentum divided.

An incision was made through the diaphragm radially from the esophageal hiatus to the costal margin and the diaphragm was completely freed from the esophagus. An excellent exposure of the entire stomach, spleen, and left lobe of the liver was obtained and no involved lymph glands were found along either curvature of the stomach. The liver was free from nodules. The stomach was partially mobilized by dividing the gastrosplenic, gastrophrenic ligaments, and the lateral attachments of the gastrocolic omentum. After this procedure the fundus of the stomach could readily be elevated to the level of the sixth rib posteriorly. The stomach was cut across about one inch below its junction with the esophagus, and the opening in it thus produced was closed with a continuous suture of No. 1 chromic catgut. A row of interrupted Lembert sutures of medium silk was used to invert this first line of

suture. The stomach was drawn into the chest and anchored posteriorly to the periosteum of the seventh and eighth ribs by means of four medium silk sutures.

The esophagus was tied off with a purse-string suture of catgut well above the tumor, and the esophagus cut across between this ligature and a Kocher clamp. An incision was made through the anterior wall of the stomach well up on the fundus. The end of the esophagus, still closed by the purse-string suture of catgut, was introduced into the stomach through this slit so that one inch of esophagus projected into the lumen of the stomach (Fig. 10). The stomach and esophagus were now united by interrupted Lembert sutures of medium silk. One row of sutures was used posteriorly and two rows anteriorly. The purse-string suture of catgut was removed from the end of the esophagus just before the last sutures were tied. Care was taken to insert the sutures in the long axis of the esophagus to avoid the constriction

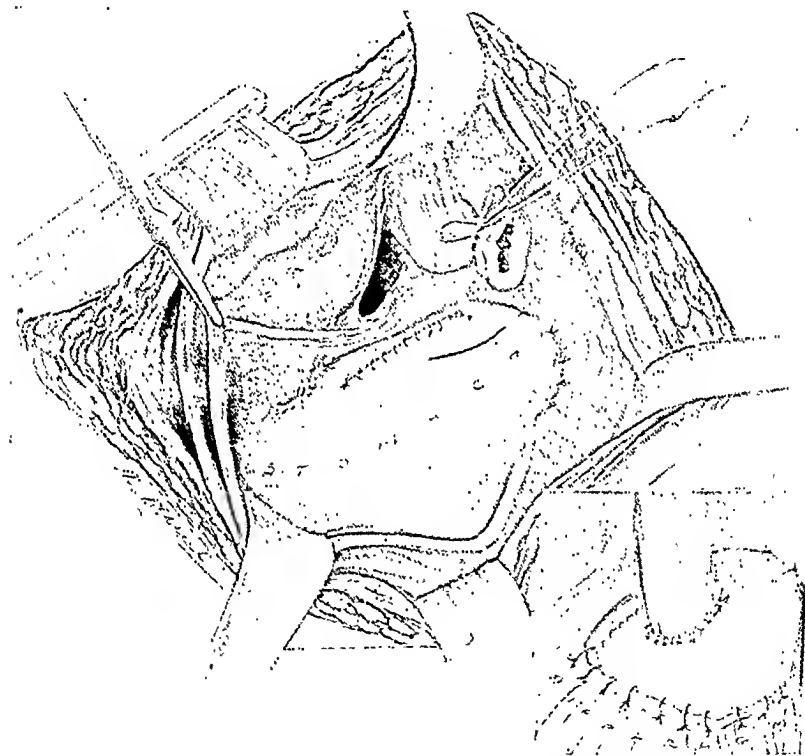


Fig. 10.—Case 2. The growth in the esophagus has been resected along with a portion of the stomach. The stomach has been closed. The solid line on the stomach shows the line of the incision in the fundus through which the end of the esophagus was introduced (contrast the direction with that in Fig. 6). The end of the esophagus has been closed with a purse-string suture of No. 00 catgut, the ends of which were left long and used to pull the esophageal stump well down into the stomach, while the latter was sutured around the esophagus. The insert shows the completed anastomosis. Note the sutures which attach the stomach to the periosteum of the seventh rib.

of the blood vessels. The line of anastomosis was almost completely covered with a tag of omentum. A stoma which would permit the introduction of almost two fingers was produced by the anastomosis. The lateral angle of the opening in the diaphragm was closed with interrupted silk sutures and the remaining edges were anchored to the stomach with interrupted sutures of the same material.

A No. 22 mushroom catheter was inserted through a stab wound in the anterior axillary line in the ninth interspace. The chest cavity was irrigated with saline

solution, and the chest wall was closed, using three kangaroo tendon sutures about the seventh and eighth ribs, continuous No. 1 chromic catgut in the superficial muscles, and fine silk in the skin. A dry dressing was applied. The lungs were well inflated with positive pressure as air was drawn by syringe through the catheter. The catheter was then attached to a continuous Wangenstein suction apparatus. A Levin tube was inserted into the esophagus through the nose and connected to another Wangenstein suction apparatus. During the operation, the patient had received approximately 2,500 c.c. of 5 per cent glucose and 700 c.c. of citrated blood.

Convalescence was uneventful. The temperature reached 102° F. on the day following the operation and fell by lysis to normal on the fourth postoperative day. Sutures were removed from the incision on the fifth and seventh days. There was no vomiting. She was given one ounce of water by mouth every two hours on the sixth day and the amount slowly increased thereafter. The catheter was removed from the chest on the ninth day, at which time the lung was found to be fully expanded and all wounds had healed without infection.

On the eighteenth postoperative day fluoroscopy showed excellent function of the esophagus. The patient had been on a liquid diet by mouth since the tenth day after operation. At lunch on the day following the fluoroscopy the patient complained of a heavy feeling behind the stomach, had some difficulty in swallowing, and regurgitated some of her food. On the next day she could swallow liquids and soft foods without difficulty if taken slowly in small amounts. A medium-sized Tucker dilator could be drawn through the anastomosis from the gastrostomy opening without any feeling of resistance. The patient was discharged to her home on June 16, 1939. By this time she was able to take complete care of herself and prepare her own meals. She was advised to have dilatations done at weekly intervals. As long as she had the weekly dilatations of the stomach, she could swallow liquids easily and also soft foods. She neglected to return for treatment after a few weeks and by the end of August, 1939, she was having trouble in swallowing anything but a strictly liquid diet.

On Oct. 2, 1939, the patient returned for a check-up examination. Her general condition was excellent. She had gained twenty-five pounds in weight and was completely free of any signs of obstruction as far as saliva and other liquids were concerned. However, she was having trouble with any semisolid food which might contain small lumps. She then admitted it had been six weeks since she had had a dilatation. Fluoroscopy showed considerable retardation in the passage of barium through the anastomosis, only a thin trickle of barium finding its way into the stomach.

The patient was taught to dilate her own stricture with Tucker dilators which were threaded on a string and pulled through the stricture from the stomach side. She did not wear a string constantly but would swallow it at will and draw it through the gastrostomy opening with a syringe. After the dilatation the string would be removed. Under this regime she has continued to swallow liquids and soft foods easily, is feeling well, and is leading a normal life.

Comment.—The mobilization of the stomach was considerably interfered with in this case by the presence of the gastrostomy, which emphasizes again that a preliminary jejunostomy is preferable to a preliminary gastrostomy. However, a gastrostomy after the operation of esophagogastrostomy has been performed is of great value and, in fact, is essential. Immediately after operation the gastrostomy prevents the extreme dilatation of the stomach which can readily result from the swallowing of air, but the inability to belch it up through a stoma which is encroached upon by edema. It is a means of keeping the stomach

free from an accumulation of fluid which might produce an unusual strain on the suture line during retching or attempts at vomiting. It offers a means of keeping up the patient's food or fluid requirements during the ten-day postoperative period when swallowing is prohibited. If a stricture forms at the stoma, it can readily be dilated by introducing dilators through the gastrostomy as was done in this case and in Case 1. Therefore, in the future it is planned to do a preliminary jejunostomy if it is necessary to feed the patient for several days or weeks before operation, and at the end of the operation of esophagogastrostomy to do a gastrostomy through the abdominal wall.

Indications of stricture were first noted on the eighteenth day after operation. The stricture has been able to be controlled by repeated dilatations, but, if these are stopped, difficulty in swallowing soon appears.

As in Case 1 the wound in the chest wall healed per primam and there was no empyema of the pleural cavity. At the time of operation there must have been gross soiling of the pleural cavity from the stomach and from the cut end of the esophagus, but the pleural cavity seemed able to contend with this, provided all clots and blood were removed from it. A large series of operations of this type performed on animals has convinced us that the esophagus can be openly anastomosed with the stomach in the thorax without fear of empyema, provided that all foreign material is removed from the pleural cavity, that perfect hemostasis is observed, and that no leakage at the suture line occurs.

SUMMARY

1. Two additional cases of successful transpleural esophagogastrostomy are reported. One patient who was operated upon in May, 1939, is alive and apparently well. The other patient died ten months after operation and, though no cause could be found at autopsy for her death, it must have been related to a stricture at the site of anastomosis which developed after operation.

2. The type of esophagogastrostomy in which the end of the esophagus is introduced into the stomach through a slit in the latter was used in both cases herewith reported, but it is not to be recommended. Stricture followed in each of the two cases in which this type of anastomosis was performed.

3. Anchoring of the stomach and the esophagus to some portion of the bony thoracic cage after they have been anastomosed is advocated in order to relieve tension on the suture line.

4. The use of continuous suction in the esophagus after esophagogastrostomy is of advantage in relieving pressure on the suture line by removing the accumulated secretions and by keeping esophageal peristalsis at a minimum.

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THE REGULATION OF CIRCULATION IN DIFFERENT POSTURES

ERLING ASMUSSEN, M.D., PH.D., E. HOHWÜ CHRISTENSEN, M.D., PH.D.,
AND MARIUS NIELSEN, M.D., PH.D., COPENHAGEN, DENMARK

(From the Laboratories of Theory of Gymnastics and Zoophysiology, University of Copenhagen)

IN 1913 Lindhard was able to show that the circulation rate is smaller in standing and sitting positions than in lying position. This result has been confirmed by later investigators who have obtained well-defined resting conditions involving a minimum of muscular activity and consequently almost the same O_2 consumption in the different postures.

In many cases the erect posture undoubtedly means a maximal stress put on the circulatory system. It is a well-known fact that especially young people with poor muscular tonus are inclined to circulatory insufficiency (decrease of arterial blood pressure, nausea, and collapse) while maintaining the standing position for a long time.

It has been our object of research to investigate if, in connection with the diminished cardiac output in standing position, any symptoms of circulatory insufficiency can be demonstrated also in cases where the arterial blood pressure remains normal and where no subjective signs of poor circulation are obvious.

METHODS AND RESULTS

The subject was placed on a tilting board and fixed in such a way that the different postures between $+60^\circ$ (head up) and -60° (head down) could be maintained without any extra muscular effort.

Fig. 1 shows the results of a typical experiment with a normal young man in good physical condition (aged 35 years; height, 188 cm.; weight, 85 kg.). The subject was tilted from horizontal to head-up position ($+45^\circ$) and sixty-five minutes later back to horizontal position. One leg of the subject was partly (8 L.) inclosed in an air-filled plethysmograph. The curve of Fig. 1 shows a large increase in volume of the leg by changing from 0 to 45° . The swelling of the leg (475 c.c.) is due to an increased hydrostatic pressure in the veins and capillaries of the lowered extremities, which will bring about a filling up of blood in the vessels, especially in the veins, and a filtration of fluid through the capillary walls. The volume change due to filtration and filling up of blood is clearly demonstrated in the plethysmogram. By tilting the subject from 45 to 0° , the plethysmogram shows a steep fall, corresponding to the amount of blood poured out from the vessels (275 c.c.), while the gradual decrease in volume is due to absorption of the filtrate.

While the oxygen consumption remains constant, the cardiac output (determined *ad modum* Grollman) shows a marked decrease (from 4.6 to 3.9 L. per minute). In the standing position* the systolic pressure is remarkably constant while the diastolic pressure is increased and consequently the pulse pressure is decreased. The pulse rate shows a sudden increase immediately after tilting from 0 to 45° and a more gradual increase during the whole period of standing; on tilting from 45 to 0°, the pulse rate suddenly drops back to the original value.

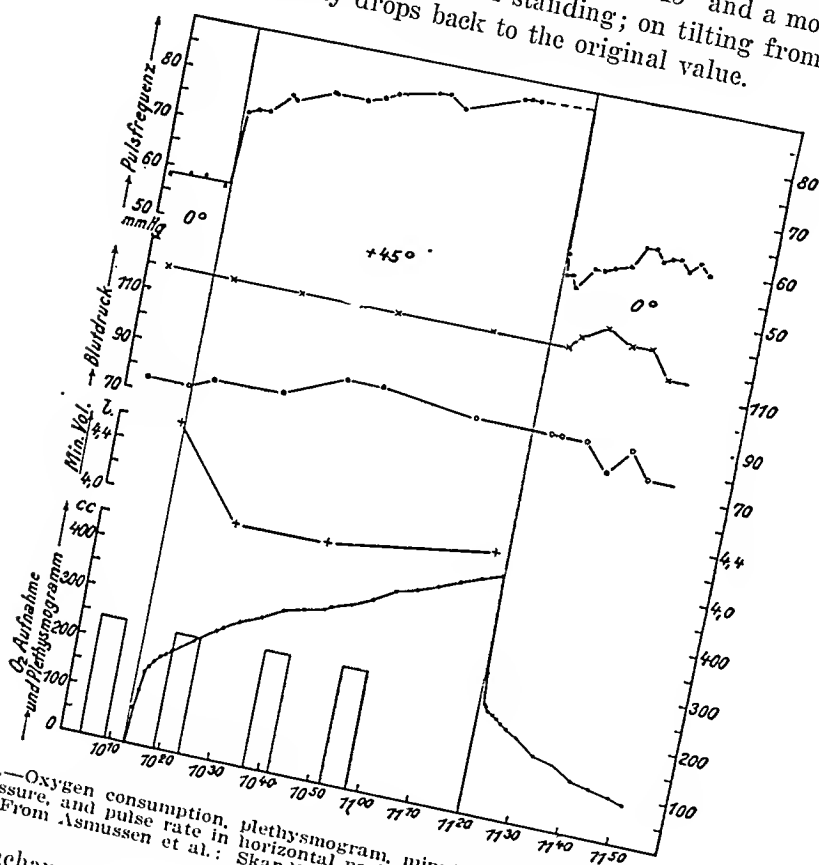


Fig. 1.—Oxygen consumption, plethysmogram, minute volume output of the heart, blood pressure, and pulse rate in horizontal position (0°) and in the head-up position (+45°). (From Asmussen et al.: *Skandinav. Arch. f. Physiol.* 81: 214-221, 1939.)

The unchanged O_2 uptake in standing makes it probable that the circulation rate, in spite of a lowered cardiac output, has been sufficient to secure a normal oxygen supply to the different tissues, but it does not necessarily mean that the circulation also has fulfilled the other claims laid to it for heat regulation, digestion, or renal function.

It may be of importance to remember that the arteriovenous O_2 difference of the arterial and of the mixed venous blood gives little or no information as to the oxygen utilization of the blood through a certain organ. In muscles the circulation rate is very likely adapted to the O_2

*The standing position here does not mean the normal standing position, but only a head-up position. The legs were practically hanging with relaxed muscles.

consumption and the O_2 utilization will therefore be high; in the kidneys, the intestines, and especially the skin the irrigation may be very high compared to the O_2 consumption and the venous blood leaving these organs therefore may have nearly the same O_2 content as the arterial blood. The high O_2 utilization found during muscular work may only mean a new distribution of the blood; relatively more blood is now passing through organs with a high O_2 consumption at the given rate of irrigation. In the same way the high arteriovenous O_2 difference found in shock conditions or during quiet standing does not necessarily indicate a slowing down of the circulation through all organs but may only show that, as the circulation cannot fulfill all claims laid to it, it is reduced through organs where it can be abandoned for some time without doing too much harm, that is to the skin, the intestines, and the kidneys, while the O_2 transport has to be kept up at a normal rate.

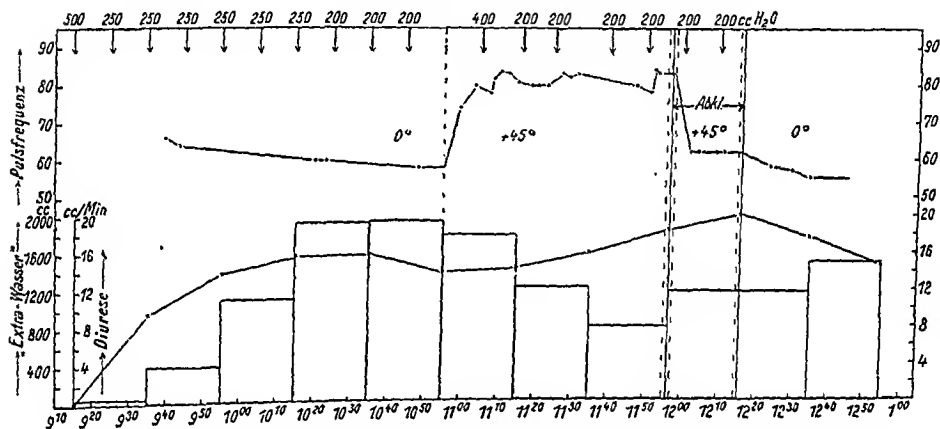


Fig. 2.—Diuresis (rectangles), extra water content of the body, and pulse rate during the drinking of water in the horizontal (0°) and in the passive standing positions ($+45^\circ$), before and after (Abkl.) cutting off the circulation to both lower extremities by pneumatic cuffs applied while the subject was in the head-down position (-20°). Arrows indicate drinking of water. (From Asmussen et al.: Skandinav. Arch. f. Physiol. 81: 214-224, 1939.)

To get some information regarding circulation to the intestine in the standing position, experiments with water intake in lying and standing positions were carried out. Fig. 2 shows some results from one such experiment. The subject was placed on the tilting board and the water intake started in horizontal position. During ninety minutes he drank a total amount of 2.6 L. of water at body temperature. The diuresis went up from a value of 0.6 c.c. per minute to 20 c.c. per minute.

The subject was now tilted to standing position (45°). In spite of the fact that the water intake continued at the same rate as before, the diuresis showed a marked drop to about 8 c.c. per minute during the following fifty minutes. The subject was now tilted to head-down position (-20°) and kept there for about one minute. Two pneumatic cuffs, in placed as nearly proximal around his thighs as possible, were then inflated to a pressure of 300 mm. Hg and he was tilted back to the stand-

ing position once more. During the following twenty minutes the diuresis increased to 12 c.c. per minute. Finally the subject was tilted back to horizontal position, the pressure on the cuffs was relieved, and the diuresis was measured during the next forty minutes. The last value was almost 16 c.c. per minute.

During the first period at 0° , the pulse rate slowed down to below 60, but the tilting to $+45^{\circ}$ induced a marked acceleration to 85 beats per minute. In the second period of standing the pulse rate was practically back to horizontal values again as a result of the transfer of blood from the lower extremities to the central vessels (see page 609).

In parallel experiments where the protein content of the blood plasmas was determined, a definite dilution of the plasma could be shown to take place during water drinking in horizontal position, while a marked concentration far above the original value took place in the standing position in spite of the intake of large amounts of water. Here again the second period of standing (with inflated cuffs) showed quite a different result, a pronounced dilution of the plasma.

The most probable explanation for the relatively small diuresis in the standing position seems to be that a large amount of the water remains in the intestines, due to a locally reduced circulation. That the circulation to the kidneys is reduced too was made probable by the fact that all three subjects showed signs of albuminuria after having maintained the quiet standing position for about one hour.

The circulation through the vessels of the skin, too, has other important functions besides the O_2 transport. In warm environment the skin circulation is much increased not due to higher O_2 consumption but due to increased demands on the heat-regulating mechanism. A large change in blood distribution therefore might be expected to produce a similar effect on the skin circulation as was the case on the circulation to the intestines.

It could be shown that when a subject in a warm room (35° C.) was tilted from horizontal to head-up position (45°) the skin circulation was much reduced, causing a drop in mean skin temperature of about 1° C. in one hour. At the same time the rectal temperature was increased about 0.5° C., due to the vasoconstriction in the skin.

The diminished cardiac output in quiet standing position is undoubtedly closely connected with the filling up of blood in the lower extremities. Primarily this accumulation of blood in the periphery will involve a diminished filling and a diminished pressure in the central veins and consequently a decreased return flow of blood to the heart. The effect of a lower pressure in the central veins to a certain extent can be compensated through an increase in pulse rate; that is, if the filling of the heart is more rapid during the first period of diastole than later on. The following figures will demonstrate a very close relation between posture and pulse rate.

Fig. 3 shows the changes in pulse rate of the same subject as mentioned before by tilting from 0 to $+60^\circ$ or -60° . In Experiments a and c the blood could freely move to and from the legs, while in Experiment b the cuffs round the thighs were inflated in the horizontal position and consequently the vascular bed in which the blood could move freely in and out was limited significantly. In Experiments a and c the pulse rate went above 80 per minute in head-up position, and in head-down position we found figures as low as 36 or 37. In Experiment b the effect of tilting was very much less pronounced.

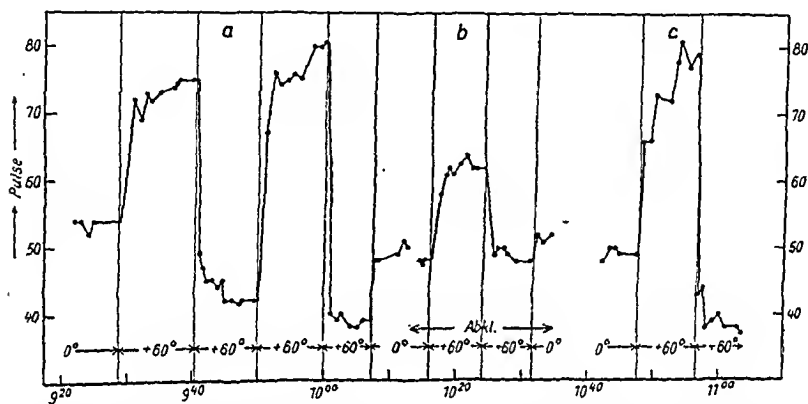


Fig. 3.—a and c, Pulse rate in horizontal (0°), head-up ($+60^\circ$), and head-down positions (-60°); b, the corresponding values after cutting off the circulation to both lower extremities by pneumatic cuffs applied while the subject was in a horizontal position. (From Asmussen et al.: *Skandinav. Arch. f. Physiol.* 81: 190-203, 1939.)

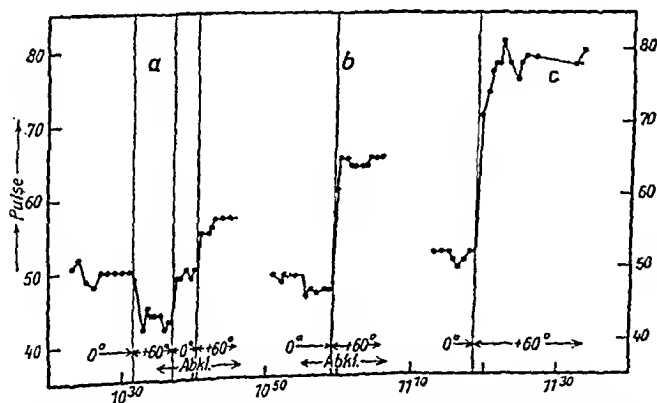


Fig. 4.—a and b, Pulse rate in different positions after cutting off the circulation to both lower extremities while the subject was: a, at -60° ; b, at 0° ; c, control determination without pressure. (From Asmussen et al.: *Skandinav. Arch. f. Physiol.* 81: 190-203, 1939.)

Fig. 4 shows the pulse rate in $+60^\circ$ (head-up): in Experiment a with "emptied" legs (the cuffs were inflated in -60° before tilting); in Experiment b with practically normal blood filling of the legs (the cuffs were inflated in horizontal position before tilting); and in Experiment c

with maximal filling of the legs (no cuffs were used). With empty legs (Experiment a) the pulse difference between horizontal and standing position ($+60^\circ$) was 5 to 7 beats per minute; with normal filling (Experiment b), 15 to 16 per minute; and with maximal filling (Experi-

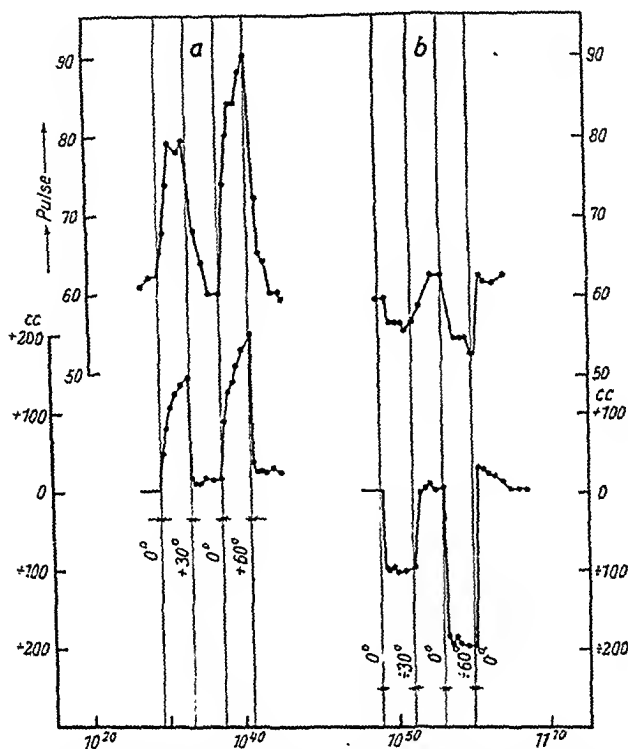


Fig. 5.—Pulse and plethysmogram (small plethysmogram): a, on changing positions from 0° to head-upward $+30^\circ$ and $+60^\circ$; b, on changing positions from 0° to head-down position -30° and -60° . (From Asmussen et al.: *Skandinav. Arch. f. Physiol.* 81: 190-203, 1939.)

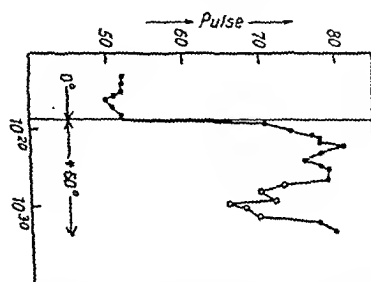


Fig. 6.—Pulse rate in the passive standing position ($+60^\circ$). Black circles indicate pulse rate while standing quiet. Open circles indicate pulse rate on voluntary contraction of leg muscles. (From Asmussen et al.: *Skandinav. Arch. f. Physiol.* 81: 190-203, 1939.)

ment c), 30 beats per minute. The subnormal pulse values in head-down position could be shown in the same way to be closely related to the amount of blood accumulated in the legs. With blood-filled legs (the cuffs were inflated in standing position before tilting to head-down posi-

tion) the pulse rate would be 50 to 55 instead of 40 or even below 40 in cases where the circulation to the legs was free (compare with Fig. 3).

Fig. 5 shows pulse rate and plethysmogram (a smaller plethysmograph was used than the one mentioned before) from the same subject in positions between $+60^\circ$ and -60° . The relation between amount of blood in the legs and pulse rate is here very clear. The most surprising result may be the fact that the emptying of the legs is so different in -30° and -60° . We expected to find very nearly the same volume in the two positions, but, as Fig. 5 shows this is by no means true; apparently it is quite difficult to make the deeper veins collapse.

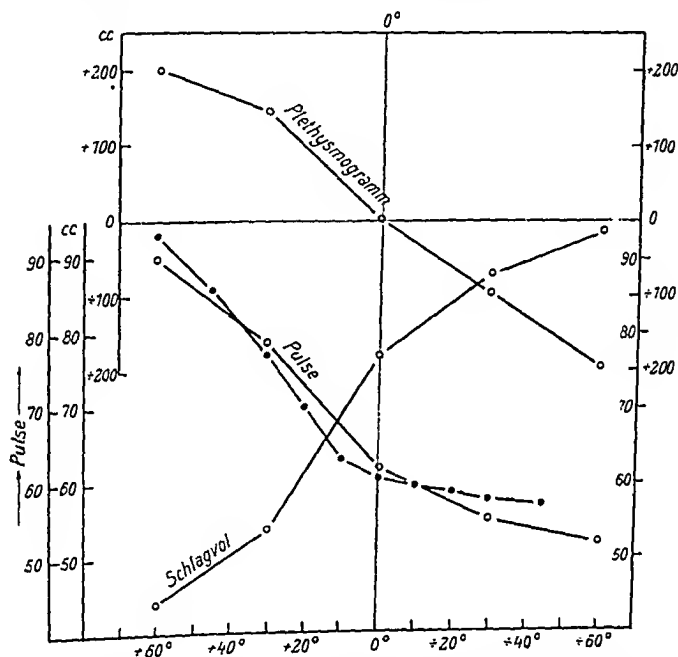


Fig. 7.—Plethysmogram, pulse rate, and output of the heart in various positions between the head-up ($+60^\circ$) and the head-down (-60°) positions. The values indicated by open circles are derived from the same experiment. The values were determined about two to three minutes after change of position. (From Asmussen et al.: *Skandinav. Arch f. Physiol.* 81: 190-203, 1939.)

Fig. 6 demonstrates the importance of muscular contractions for the circulation. The subject has been tilted to head-up position ($+60^\circ$) and in a few minutes the pulse rate went up from 50 to 80. The subject now started to make static contractions of his leg muscles and the next countings showed a pulse of 65 to 70. As soon as the contractions stopped, the pulse rate went up to 80 again. The muscle contractions forced the blood out of the veins back to the central vessels.

In Fig. 7 measurements of leg volume, pulse rate, and stroke volume from the same experiment were plotted together. The stroke volume varied between 45 c.c. in $+60^\circ$ (head-up position) and almost 100 c.c. in -60° (head-down); even larger changes are shown in Table I.

TABLE I

O₂ CONSUMPTION AND CIRCULATION IN DIFFERENT POSTURES

| POSTURE | ARTERIOVENOUS O ₂ DIFFERENCE C.C./L. | O ₂ CONSUMPTION C.C./MIN. | CARDIAC OUTPUT L./MIN. | PULSE RATE | STROKE VOLUME (C.C.) |
|---------------------|---|---|------------------------------|----------------------------|----------------------------|
| +60° (head-up) | 57, 62 Avg. 60 | 240, 245 Avg. 243 | 4.05 | 79, 98, 91, 100 Avg. 92 | 44 |
| +45° (head-up) | 62, 61, 58 Avg. 60 | 237, 242, 242 Avg. 241 | 4.0 | 77, 80, 81 Avg. 79 | 51 |
| 0° (horizontal) | 51, 55, 54, 49, 50 Avg. 52 | 249, 249, 257, 242 Avg. 249 | 4.8 | 55, 57, 52, 54 Avg. 55 | 87 |
| -60° (head-down) | 54, 49, 51 Avg. 51 | 250, 252 Avg. 251 | 4.9 | 45, 38, 41, 45 Avg. 42 | 117 |

The close connection demonstrated between peripheral blood distribution and pulse rate gives a strong support for the opinion that the changes in pulse rate can be regarded as essential parts of a mechanism securing an adequate circulation rate. In head-down position we found that the pressure in the central veins (method of Henderson) was 10 to 15 cm. of blood higher when measured with empty legs than when measured with blood-filled legs. The higher venous pressure found in experiments with emptied legs must be due to an increased filling of the central veins. The blood that has been forced out of the lower extremities seems to have moved to the central vessels, increasing the pressure here and diminishing the air space in the thorax by about the same volume (Table II).

TABLE II

VITAL CAPACITY WITH "EMPTY" AND "FILLED" LEGS IN HEAD-DOWN POSITION (-60°)

| SUBJECT | E. A. | E. H. C. | T. S. |
|---|-----------------------------------|-----------------------------------|-----------------------------------|
| Vital capacity with "filled" legs (L.) | 4.83 4.88 4.81 Avg. 4.84 | 5.04 5.20 5.10 Avg. 5.11 | 4.67 4.62 4.63 Avg. 4.64 |
| Vital capacity with "empty" legs (L.) | 4.35 4.33 4.35 Avg. 4.34 | 4.60 4.69 4.61 Avg. 4.63 | 4.23 4.18 4.28 Avg. 4.23 |
| Difference in vital capacity with "filled" and "empty" legs (L.) | 0.50 | 0.48 | 0.41 |

The mere fact that the venous pressure is kept high and the air space of the lungs is kept low as long as the head-down position is maintained shows that the blood from the legs is not taken up by real blood depots.

If the pulse rate of the standing or horizontal position were maintained in head-down position, with increased venous pressure and consequently increased diastolic filling and increased stroke volume, the cardiac output and the arterial pressure would increase and would be kept at an unnecessarily high level. By decreasing the pulse rate, the cardiac output can be kept normal in spite of the increased venous pressure and increased stroke volume, provided only that the diastolic filling

does not increase in proportion to the longer diastolic period. From that point of view it is quite natural to look upon the lower pulse rate in head-down position as a compensation for the increased pressure in the central veins, and in the same way to take the fast pulse rate in the standing position as a compensatory arrangement against a decreased pressure in the central veins.

An increased pressure in the central veins, according to Bainbridge, should induce a faster pulse rate. The pulse acceleration found during muscular exercise is very often explained as being brought about in that way. As our results show, we have not been able to find any sign of a Bainbridge reflex and under these circumstances it would be very unfortunate if it really existed; in head-down position it would counteract the regulatory arrangements put into action to secure a normal cardiac output and a normal arterial blood pressure. The experimental proofs that a Bainbridge reflex is released by an increased pressure in the central veins are not very convincing.

The pulse curves show that the changes in heart rate take place immediately after tilting, which indicates that they must have the character of a reflex.

In the arteries close to the heart only small changes in pressure will take place by tilting the subject, while the pressure in the more peripheral arteries may change significantly according to the distance from the heart. Consequently small changes only will take place in the aorta and rather larger changes in the sinus carotidis; therefore one might expect that the high pulse rate in the standing position might be due to a decreased pressure in the sinus and the low pulse in head-down position be due to an increased pressure in the sinus. The pressure changes should be the direct effect of a lifting or lowering of the sinus in relation to the heart. The results of our experiments give a strong indication against that explanation. As shown by Fig. 3, practically the whole effect of tilting could be obtained simply by changing the amount of blood in the central vessels and here the relation between heart and sinus is unchanged. This fact also makes it very unlikely that the low pulse rate in head-down position should be due to an increased pressure in the fourth ventricle of the brain brought about by hydrostatic forces in that position.

The reason for the pulse changes cannot be a primary change of pressure in the arteries but must be correlated to the shifting of blood from or to the central veins. However, a difference in venous pressure, as already pointed out, can influence the arterial pressure via the cardiac output. If a decreased venous pressure brings about a lower cardiac output it also will give a lower arterial pressure; via the pressosensible mechanism the pulse rate will increase as much as possible to compensate the low filling pressure of the heart and secure an adequate cardiac output.

The results of the following experiments will show that a close dependence exists between arterial blood pressure and heart rate and can be demonstrated not only on operated animals but also on human beings with the regulation of circulation intact. Fig. 8 shows systolic blood pressure and pulse rate for three normal subjects in experiments where

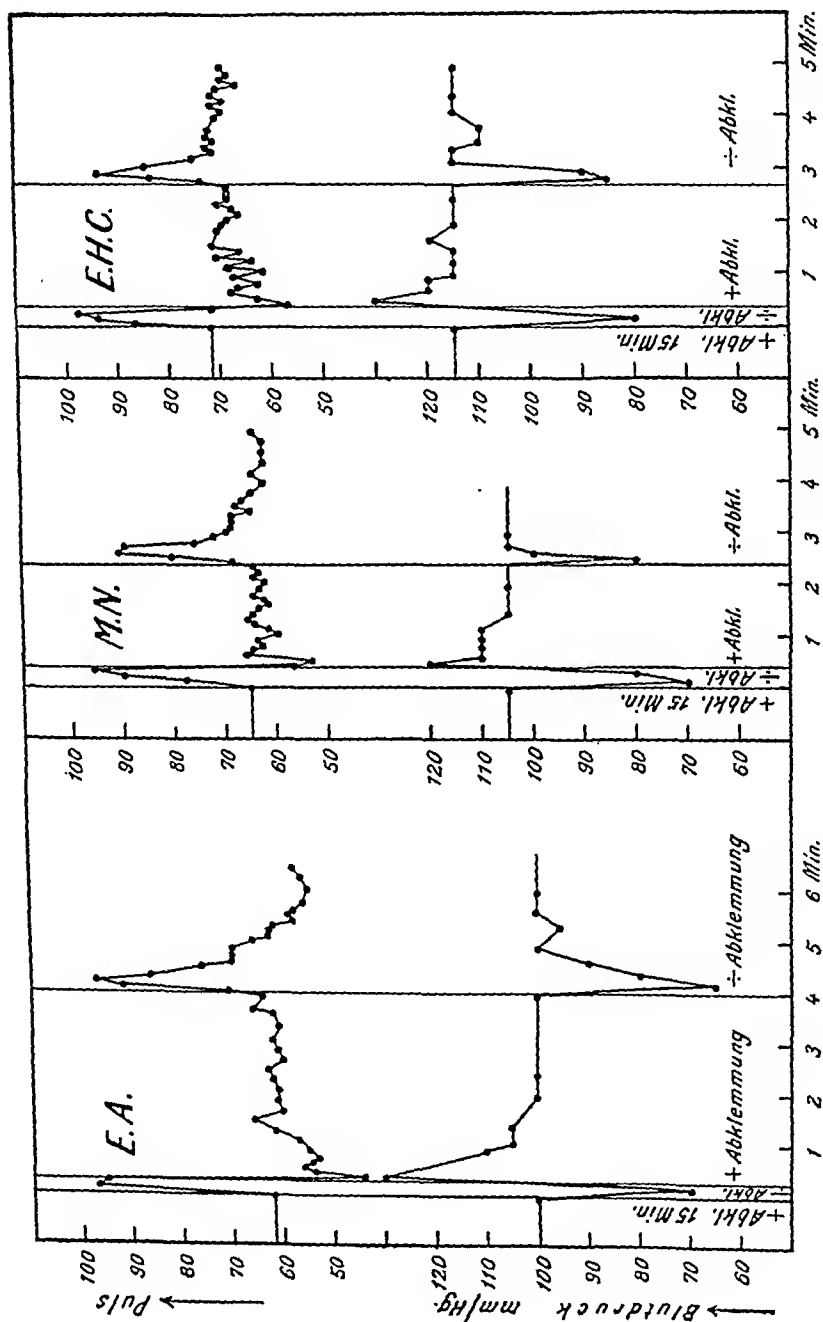


Fig. 8.—The blood pressure and pulse rate on repeated cutting off and opening of the circulation to both extremities. (From Asmussen et al.: Skandinv. Arch. f. Physiol. 79: 32-38, 1938.)

marked changes in the functions mentioned were produced by a severe anoxemia in the leg muscles. The subjects were sitting in an easy chair and pneumatic cuffs round the thighs were inflated to a pressure of 300 mm. Hg for fifteen minutes. The pressure was then released for ten to twenty seconds and suddenly put on again and kept on for a few minutes before it was released finally. As Fig. 8 shows, the first release of pressure will induce a steep fall in blood pressure and simultaneously a marked increase in heart rate, and, when the circulation to the legs is blocked the second time, the blood pressure will suddenly rise above the normal value, while the pulse rate will reach subnormal values. In these experiments the pressure regulation has not been sufficient to compensate for the effect of a sudden and large demand for blood to the anoxic area in the leg muscles and the arterial pressure drops down;

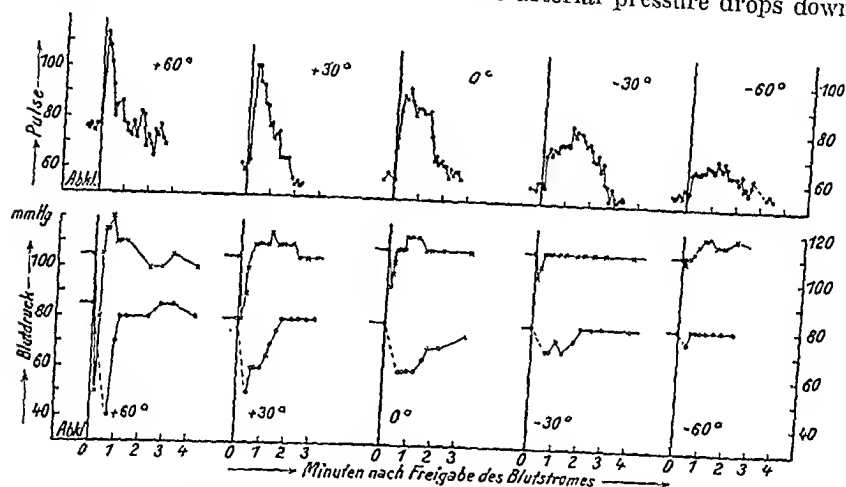


Fig. 9.—Pulse rate and blood pressure in reactive hyperemia in different positions of the body. (Release of pressure on the blood stream in both lower extremities after about fifteen minutes of pressure.) (From Asmussen et al.: *Skandinav. Arch. f. Physiol.* 81: 204-213, 1939.)

the pressosensible reflexes are then released and as a part of the compensatory mechanisms the pulse rate is increased. If the fast blood stream to the anoxic areas is suddenly stopped, the blood pressure goes up and consequently the pulse slows down below normal. In the following experiments this procedure was used to test the effectiveness of blood pressure regulation in different postures.

Fig. 9 shows the result of such experiments. The subject was placed on the tilting board and after a sufficient period of rest (one hour) the cuffs round the thighs were inflated and the subject was tilted to the desired posture. The pressure was then released fifteen minutes later and arterial blood pressure and pulse rate were registered during the next minutes. Fig. 9 shows that the pressure control is almost perfect in -60° (head-down position) and very severely affected in +60° (head-up), but in all cases the normal pressure was established again very soon.

In the experiment shown in Fig. 10 the period of anoxemia lasted twenty minutes, and, when the pressure was released in $+60^{\circ}$, the subject showed the normal drop in blood pressure and increased heart rate; a normal pressure value was reached in about one minute, after which, however, a second drop in pressure took place, the subject almost fainted and had to be tilted back to horizontal and even to head-down position before the pressure again reached normal values. It is very interesting and perhaps a fact of great significance that the second drop in pressure was not, as usual, followed by an increased heart rate.

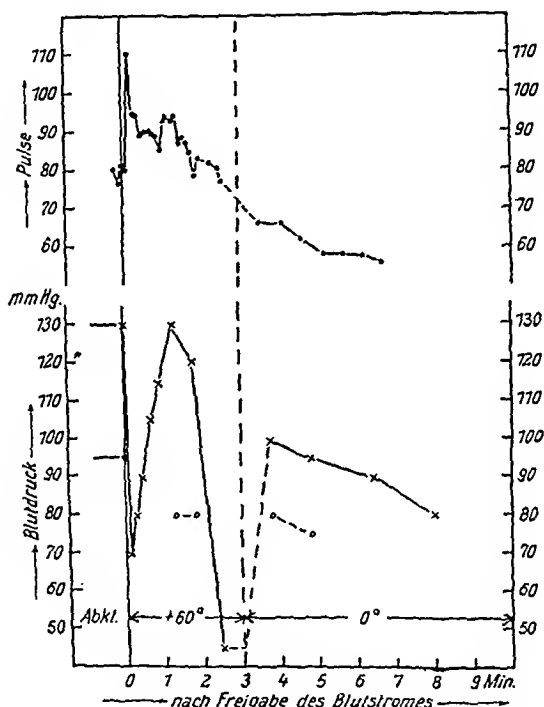


Fig. 10.—Pulse rate and blood pressure after release of pressure on the blood stream with subject in the upright position ($+60^{\circ}$). (Pressure on both lower extremities for twenty minutes.) (From Asmussen et al.; Skandinav. Arch. f. Physiol. 81: 204-213, 1939.)

The plethysmographic records showed that the filling up of blood in the lower extremities was of the same magnitude in cases where the effect of tilting was combined with anoxemia in the leg muscles. In the latter case the filling up took place much faster; in ten to twenty seconds the same swelling of the legs had taken place that would take five minutes in the case of tilting only.

CONCLUSIONS

Our experiments indicate that the circulation rate in quiet standing is on the lower limit of what is really desirable and that, even if the fast pulse rate in the standing position in itself is no sign of insufficiency, it

indicates on the other hand that some extra stress is put onto the pressure-regulating mechanism.

A diminished cardiac output during quiet standing has to be looked upon as a sign of insufficiency, even if the O_2 consumption and the arterial blood pressure remain normal. The vessels of the lower extremities are distended by hydrostatic forces; a large amount of blood remains there and consequently the filling and pressure of the central veins get too low to secure an adequate filling of the heart and a normal cardiac output. Through an increased heart rate and through compensatory contractions of the vessels in certain organs (e.g., in the intestines) a normal arterial blood pressure might be obtained. However, it must be remembered that a diminished circulation rate to these organs with partly contracted vessels locally may have an unfavorable effect. It may be of great importance that circulatory insufficiency due to a peripheral dilation of the vessels or to a loss of blood can be counteracted by an elevation of the lower extremities. The autotransfusion of blood that can be made in this way may be of great significance. In cases where a circulatory insufficiency due to a disproportion between the total blood volume and the capacity of the vessels is obvious, any posture where hydrostatic forces can induce an increased filling of the vessels of the lower extremities should be avoided. Even a small decrease in cardiac output may mean a rather severe insufficiency of the circulation of certain organs. The beneficial effect of the reclining position to a great extent may be due to the abundant blood supply to the different organs obtainable in that position.*

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*A more detailed documentation of the above-mentioned facts and references to the literature are to be found in *Skandinavisches Archiv. für Physiologie*, 1938 and 1939.

TUMOR EMBOLISM OF THE COMMON FEMORAL ARTERY, TREATED BY EMBOLECTOMY AND HEPARIN*

KARL-ERIK GROTH, UPPSALA, SWEDEN
(From the Surgical Department of the Hospital of the Royal Academy)

ACCORDING to all experience, occluding embolisms of the arteries of the circulatory system resemble each other in two respects especially: (1) with reference to the source, which apart from rare cases of so-called paradoxical embolism is generally the left half of the heart and occasionally the central parts of the aorta; and (2) with reference to the material in the embolus itself, which usually consists of centrally formed thrombus matter.†

The case related below differed in both these respects: (1) the source of the embolus was undoubtedly the lungs; and (2) the material in the embolus mainly consisted of tissue of a malignant tumor. In addition to its interest from an etiological point of view, the case also was interesting therapeutically, as certain possibilities had to be considered with reference to the treatment, which will be discussed below; and as heparinization during and after the operation proved to be of great value, a question that is of great current interest. In the clinical description of the case I shall discuss the operation and the subsequent course in detail in order to demonstrate as adequately as possible the remarkably favorable effect of the heparinization.

CASE REPORT.—Mrs. S. K., born on Aug. 13, 1903 (Diary No. 796/39). The earlier history, the main features of which will be seen in Fig. 1, is of interest in this case. The patient enjoyed good health and attended to her household work until the beginning of 1932, when symptoms from the lungs appeared. On Feb. 11 an x-ray of the lungs disclosed several morbid spots in the parenchyma (Fig. 2). These spots were interpreted as metastases of the sarcoma in the right tibia (Prof. Hugo Laurell), for which the right leg had been amputated in 1937. She then remained at home, confined to her bed, until Feb. 27, when symptoms of embolism in the left leg made their appearance in connection with an attack of coughing.

The embolism started insidiously at about 1:00 P.M. when the patient experienced slight pains in the lumbar region and, after a while, a heavy feeling in the left leg. By degrees, sensations of cold and numbness set in and, after a few hours, a moderate aching pain. This pain increased toward the evening, a physician therefore being called in. His diagnosis was embolism; he gave morphine and referred the patient to the hospital.

On Feb. 27, 1939, at 9:00 P.M. the general condition was but little affected. In good flesh. There was distinct cyanosis of the lips and slight dyspnea when speaking. The temperature was 37.2° C., pulse, 100/min., regular, well filled, heart action, unimpaired.

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†In this connection the cases in which a foreign body has entered the circulatory system from without and started wandering are not taken into consideration.

In the left leg and foot there were moderate, aching pains, with sensations of cold and numbness in the limb. The picture presented was typical of occluding embolism of arteria femoralis communis, the circulation in the leg being stopped. The oscillometer recorded nothing at the middle of the thigh, but the pulse could be palpated up at the groin.

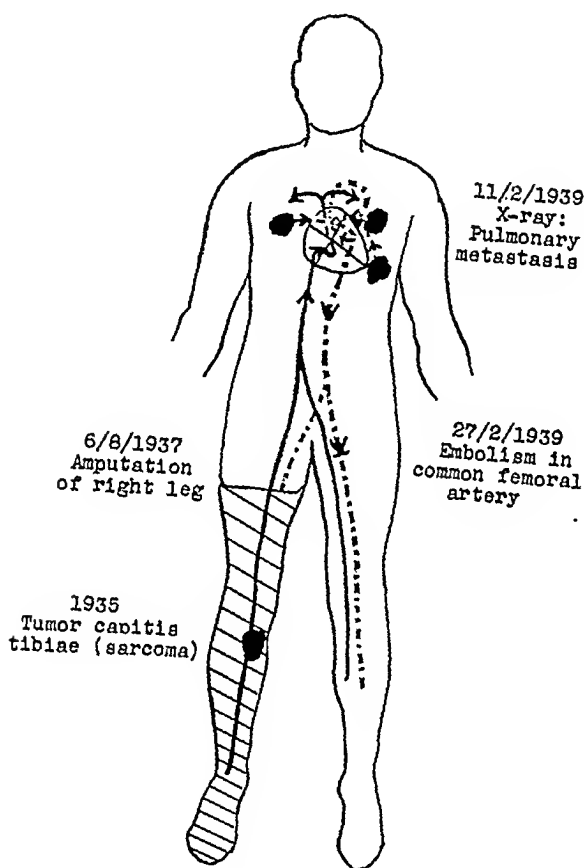


Fig. 1.

The diagnosis of embolism of the left common femoral artery was considered quite definite. It was also thought certain that whatever steps were taken could only be of a palliative character, since the patient's lung metastases would probably cause death in a fairly short time. The disturbance of the circulation in the leg was so severe that it undoubtedly would lead to gangrene, possibly amputation. Considering the fact that the patient both clinically and roentgenologically lacked all signs of heart diseases and that large sarcoma metastases had been demonstrated in the lungs, there was furthermore the possibility of tumor embolism developing, with the consequent results of such embolism. Under these conditions it could not be considered correct to start a vasodilator treatment, for instance with eupaverin,

especially since the effect of such a treatment is very doubtful when the embolus is situated as in this case. Considering the patient's youth and, in spite of the present ailment, her fairly good general condition, it was thought well justified to suggest embolectomy with a view to sparing her the suffering associated with gangrene and the possible development of a tumor in the remaining leg. Furthermore, it was impossible, of course, to know how long she might live with her lung metastases.

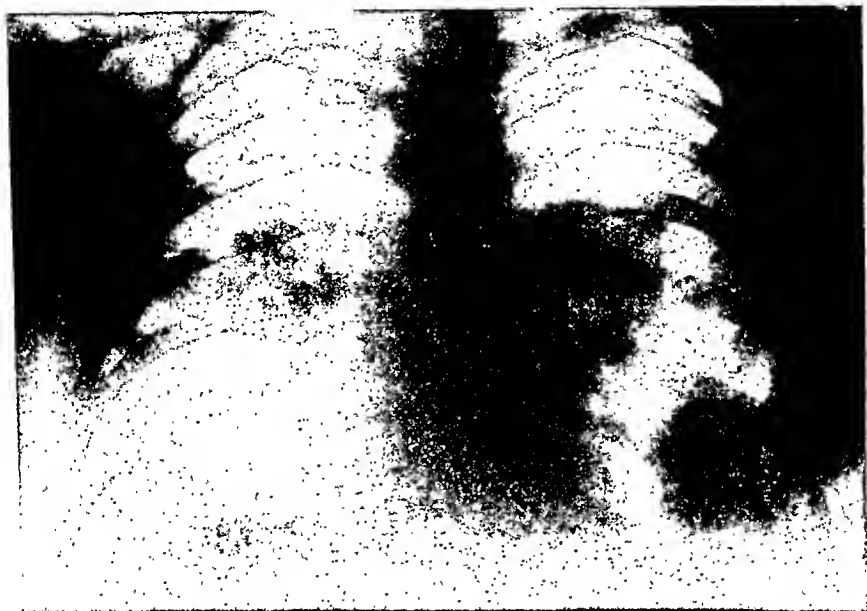


Fig. 2.—X-ray, taken Nov. 2, 1939, showing pulmonary metastases.

Embolectomy of the left common femoral artery with removal of secondary post-embolic thrombus, and intra-arterial injection of heparin were performed at 11:30 P.M. (about ten hours after the symptoms appearing). Local anesthesia with novocain and adrenaline was used.

The femoral artery was exposed from Poupart's ligament some distance down the thigh. It was of normal width and pulsated strongly about 2 cm. below the ligament. Farther down it was of the same width but felt filled with solid matter down to the spot where the deep femoral artery branched off. Toward its distal end the artery was distinctly thinner (about the width of a pencil). It was not collapsed but was bluish, and felt firm when palpated; evidently it was filled with a secondary postembolic thrombus. After the ordinary preparations, an incision was made above the lower pole of the embolus, the upper part of the secondary thrombus simultaneously being exposed. The stream of blood was not strong enough to press out the embolus, and the upper part of the vessel, therefore, was drawn tight. The thrombus was seized carefully with a forceps, and, when cautiously removed in the central direction, a piece, about 7 cm. long, was brought out. The embolus itself was then easily massaged out, the peripheral end of the artery being closed. There appeared meaty, grayish red masses, which did not resemble a thrombus. A spurting stream of blood followed, which was allowed

to rinse the wound. When the artery had been closed on either side of the incision, with the aid of soft rubber tubes, there occurred strong collateral bleeding from *arteria profunda* which was closed with a third tube. After controlling the stream of blood, the artery was sutured. The blood pulsated past the arteriotomy and the circulation in the leg and foot improved, the toes remaining white, however. After a while the pulsation in the artery ceased and it again felt filled. The suture was undone, and, upon massaging the artery, clots and fragments of the embolus appeared, similar to those already removed, a stream of blood then spurted out. The suture, which had to be reinforced to make it tight, was renewed. This time there were again but temporary pulsations in the artery, but the passage was opened down to the deep femoral artery and the upper tube therefore moved below that artery. It was decided that a renewed try should be made a little farther down and that, when the obstacle in the artery had been removed, eupaverin should be injected. This had been done by Denk experimentally in dogs and in one or two cases (according to his last publication, 1938) in man without any detrimental secondary effects being observed. When some red thrombi had been removed

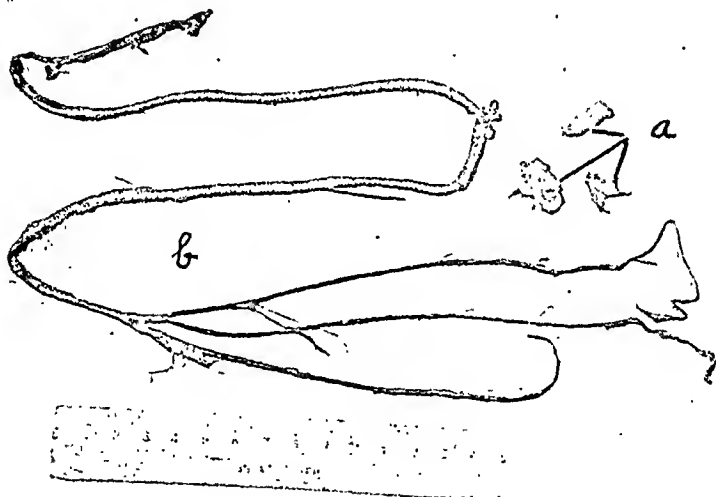


Fig. 3.—Emboli of tumor tissue (a) and postembolic thrombus (b).

by an incision farther down and a spurting stream of blood had appeared and the suture made, two ampoules of eupaverin (0.06 Gm.) were slowly injected into the artery. The patient stated almost immediately that she felt an acute, smarting pain down the leg. The pulsation passed the last suture and the color of the foot improved slightly, though for a short while only, the pulsations below the sutures also ceasing rather rapidly. It was presumed that there was an occluding thrombus farther down and that it was added to on the proximal side after each cleansing. Upon palpating the distal part of the artery, the impression was created that it was filled with a solid mass. Another incision was thus made farther down; there was no bleeding; after massaging out fresh clots from the central part, a spurting stream of blood appeared, but there was still no bleeding from the peripheral part. A paraffined probe was introduced a short distance into the peripheral part; it encountered no resistance, but when it was pulled out the upper end of a black-red thrombus appeared and was seized with a forceps and about 75 cm. pulled

out (Fig. 3). It felt rather firm and had apparently been in the artery the whole time. It was followed by fairly heavy bleeding. After renewed massage on the central side, the peripheral tube being stopped, new fresh clots appeared followed by a spurting stream of blood. A suture was made, whereupon 1 ampoule of eupaverin (0.03 Gm.) was injected into the artery, also this time followed by an acute, smarting pain down the leg. The foot and toes immediately improved in color and the circulation appeared to have started afresh. Pulsations were felt, too, as far in the peripheral direction as could be ascertained with the finger. While awaiting developments, the artery was dabbed with sodium citrate, but after about ten minutes the circulation was evidently impaired; the foot gradually became entirely white, the pulsations ceased, and around the sutures the artery was felt to be filled with soft clots. It was thus evident that no satisfactory result could be anticipated, because of the decided tendency to thrombosis; postembolic thrombosis had occurred throughout practically the whole limb, and repeated arteriotomies within a short while had been followed by clotting around the sutures, injections of eupaverin into the artery not being sufficient to prevent this clotting. Under these conditions it was considered of no avail to make additional tries to restore the circulation in the artery unless the blood's tendency to coagulate could be mastered. It was thought that heparin offered a solution worth testing, and, since after four arteriotomies lasting well over one hour the patient's general condition was practically unchanged and good, it was decided that another endeavor should be made. It was presumed that the chances of a satisfactory result would be best if the passage in the artery was first restored and heparin immediately injected into the artery on the central side of the sutures. The middle suture was severed; clots were massaged out from both sides, followed from above by a spurting stream and from below by a profuse stream of blood; the opening then was sutured and made completely tight. A short distance above the upper suture there was immediately injected, very slowly, 2 c.c. of a 5 per cent solution of heparin (100 mg.*). While the injection was being performed, a little blood could be seen starting to ooze out between the sutures in the artery and even in the holes from the eupaverin injections, which previously had been quite dry. A little while after this injection, 1 ampoule of eupaverin was also given. The oozing bleeding gradually ceased. The pulse continued, the foot had a good color and felt rather warm, and the patient could move her toes. The operation was concluded.

Subsequent Course.—After the operation the oscillometer gave small registrations across the calf. The leg and foot were subjectively and objectively warm. The patient had no pains. The general condition was satisfactory. She was given cautious heat treatment along the limb; eupaverin was administered intravenously during the night, 1 ampoule every other hour, and during the following days three times daily; herparin was given intravenously three times daily, 1 c.c. (50 mg.) for 3 days.

The circulation in the limb remained. The day after the operation there were no subjective troubles; the foot felt warm, and sensibility and motility were satisfactory; the strength of the ankle joint was diminished, however, especially when bent backward. The muscles of the calf were firm, indicating an ischemic injury as a result of the ar-

*Milligram of standard heparin according to Jorpes, corresponding to 500 and 100 cat units respectively, according to the earlier and later designations used by Murray and Best.

terial stoppage which lasted for more than ten hours. Fig. 4 shows the skin temperature on the plantar surface (measured according to Ipsen) during the first days following the operation. The oscillometric

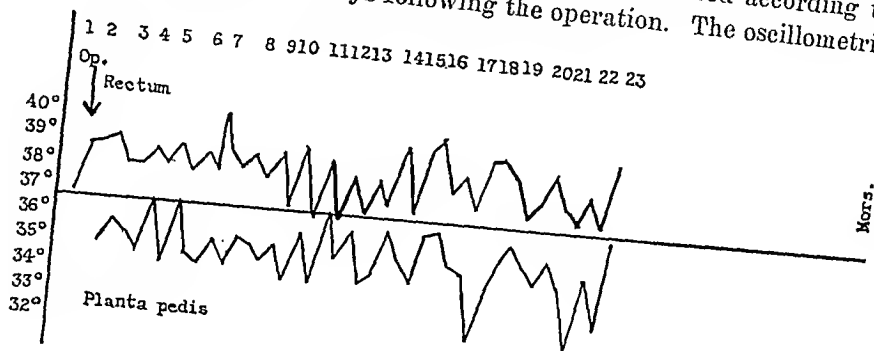


Fig. 4.

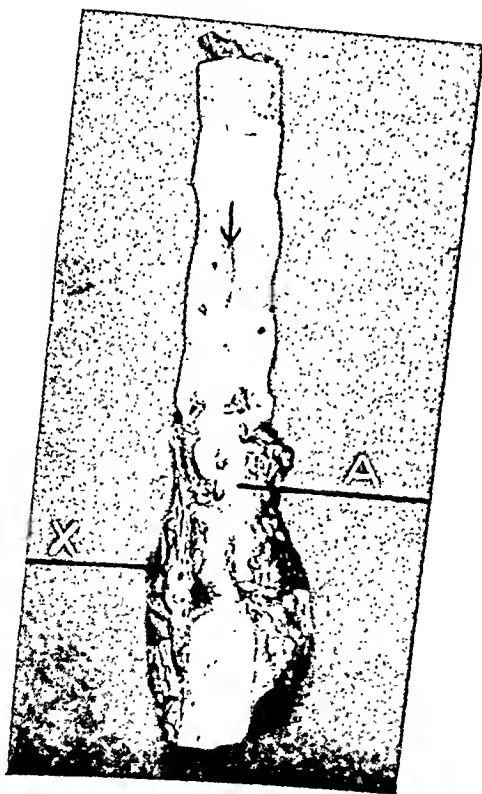


Fig. 5.—One of the incisions in the femoral artery with small thrombotic deposits on the intima (X); mouth of the deep femoral artery, Δ.

index for the calf was determined repeatedly and found to be 1.5. The wound healed per primam and the heparin treatment caused no secondary hemorrhage or other disturbance of the healing.

During the next few weeks the condition was fairly satisfactory, in spite of a fever and coughing, which was sometimes aggravated to bad attacks with dyspnea and cyanosis. On a few such occasions the patient brought up rather large solid lumps of tumor tissue, indicating a decidedly destructive growth on the part of the lung tumors, but there appeared no symptoms of new emboli. The condition of the limb remained unchanged and good, the motility even improved a little as a result of medicomechanic treatment. Finally the condition grew worse fairly rapidly in a few days and the patient died on March 31, one month after the embolism.



Fig. 6.—Heart and lungs from behind. Pulmonary veins occluded by tumor tissue (X); open pulmonary veins, Y; arteria pulmonalis, A.P.; atrium sinistrum, A.S.

The post mortem^o in the main confirmed the clinical findings and I shall discuss only the findings in the femoral artery, lungs, and heart. Fig. 5 shows the femoral artery opened. The passage is free, but at the sutures the caliber is slightly constricted and in those places there are also some minor thrombotic deposits on the intima. The artery is surrounded by a rather thick periadventitial cicatricial tissue, a matter that has of late attracted a certain amount of attention (Fiolle, Haimovici, and others), and which has been indicated to be the cause of circulatory disturbances after successful embolectomies. In this case it apparently had no detrimental effect. The femoral circumflex arteries were filled with masses of thrombi.

^oPost mortem performed by the Pathological Institute of the University of Uppsala.

Fig. 6 shows the lungs and heart from behind. The left auricle and the pulmonary veins are cut up and the pulmonary artery cut off where it branches. On either side the pulmonary veins are occluded by tumor tissue protruding from their mouths in the shape of rounded plugs. One branch is free on either side. On one side a tumor had broken into a main bronchus and on the other out into the pleura. The ventricles contained no thrombi, and, apart from its being slack, the heart displayed no anatomical changes.

Histologic Examination.—The histologic examination proved that the embolus consisted of tumor tissue together with thrombus matter, which was a possibility anticipated clinically. Fig. 7*A* shows a section through the embolus; the tissue consists of a giant-celled sarcoma, the structure of which fairly well resembles the primary tumor as it appears in an old section from a trial excision in 1937 (Fig. 7*B*); the figure also shows a piece of a tumor that was coughed up (*C*).

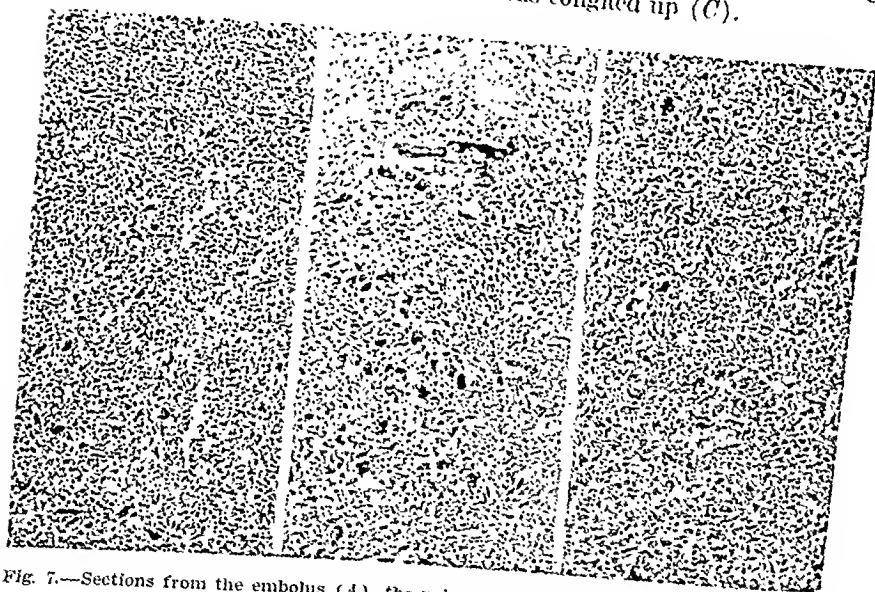


Fig. 7.—Sections from the embolus (*A*), the primary tumor in the right tibia (*B*), and a piece that was coughed up (*C*).

DISCUSSION

Source of Embolisms of the Arteries of the Circulatory System.—It was mentioned in the introduction that the commonest source of embolism of the arteries of the circulatory system is the left half of the heart (Bull, Key, Petitpierre, Groth, and others), where thrombi are formed, especially in various kinds of heart diseases, and are then thrown out. Sometimes the formation of thrombi on atheromatous wounds in central parts of the arterial system have caused embolism in more peripheral parts.

In rare cases thrombosis in the venous system or in the right auricle may have caused embolism of the arteries of the circulatory system, so-called paradoxical embolism. The first condition under which this occurs is, of course, a communication between the two halves of the heart, a foramen ovale apertum, or a defect in the septum ventriculorum (Louis). A persistent ductus arteriosus botalli is also a theoretical possibility, but this anomaly is so rare that it may be practically excluded. In spite of the fact that foramen ovale apertum in post-mortem material is so common as to be found in 30 to 35 per cent of all cases (Hirschboeck, Koritschoner), transposition of thrombi from the right to the left auricle is probably quite rare; for, as a rule, foramen ovale has the character of a canal running obliquely through the septum atriorum, preventing a passage that way as its walls are pressed together by the pressure in the auricles. Experimentally, Gross demonstrated that emboli may pass through if the pressure in the right auricle is greater than in the left, but not when the pressure conditions are the other way round, this depending on the above-mentioned valve mechanism. A difference in pressure between the auricles favorable to paradoxical embolism arises as a result of pulmonary embolism (Haggart, Walker, Parkinson), and this facilitates a fairly reliable diagnosis of paradoxical limb embolism (Hirschboeck). In 1881 Zahn described the first case in which a thrombus was found just in the foramen ovale, and subsequently several such cases have been published; lately, for example, by Hirschboeck, Taylor, and Koritschoner, the last having collected twelve cases. In 1929 Key mentioned some cases treated by embolectomy in which the embolus was presumed to be of a paradoxical type; but, upon a closer study of them, it was found that in most of the cases objections could be raised against the presumption. On the basis of Bull's examinations, Key takes up a deprecatory attitude toward the possibility of paradoxical embolism, but he does not dispute the possibility of its having occurred. Nyström has published one case of embolectomy, among others, which from all appearances was paradoxical embolism. It would seem as if the above-mentioned cases in which a thrombus has been discovered in the foramen ovale are strong supports for the occurrence of paradoxical embolism. The objection has been raised that the thrombi may have been formed in the foramen ovale, but the findings published, e.g., by Koritschoner, and illustrated with photographs, seem to furnish convincing proof that we are concerned with the passage of an embolus.

The pulmonary veins may possibly be another source of embolism in the circulatory system, which has also been considered (Key, Lund). However, I have found no mention in the literature of any case of diagnosed occluding embolism in the circulatory system in which that

source was established. The case described above is thus of interest as the embolism undoubtedly emanated from the lungs.

Type of Embolus.—There is probably no doubt but that emboli removed by operation as a rule consist of thrombus matter, and it is presumably for that reason that they are generally not subjected to a microscopic examination. The histologic examination of the embolus described above, disclosed it to consist of sarcomatous tissue, on which thrombus matter had been deposited. It is in itself not uncommon that small fragments of malignant tumors get into the blood vessels and are transported with the blood, but it is probably a rare occurrence that large pieces, as in this case, are removed and cause a stoppage in one of the large arteries of the circulatory system. As far as I have been able to ascertain, the literature contains no record of such a case having been subjected to embolectomy. The case thus shows that it is necessary to count on the possibility of embolic tumors, since this possibility should be of great importance when choosing the method of treatment.

The wandering of the sarcoma in this case is interesting. It would appear to be certain that the pulmonary tumors were metastases. They were multiple and displayed good histologic agreement with the primary tumor. It is considered typical for sarcomas that they spread by way of the blood vessels. The primary tumor in this case was localized to caput tibiae and symptoms began to appear in 1935. Having spread via the venous system, lung metastases made their appearance, in the beginning of 1939, the disease then spreading to the left leg by way of the arterial system. The decidedly destructive growth of the pulmonary tumors and a certain brittleness of the tumor tissue undoubtedly have greatly facilitated the last-mentioned spreading; i.e., the embolism. Thus, tumors grew widely into bronchi and into the main branches of the pulmonary veins. The direct cause of fragments of intruding tumors, both in the bronchi and in the veins, being released and partly coughed up, partly flung out into the arterial system as emboli, was undoubtedly a coughing attack; for then, as is well known, the lungs are rapidly and strongly compressed and the pressure increases in bronchi as well as veins and endeavors to empty them. A plug of a tumor penetrating into the lumen is then easily broken off and flung out.

Treatment.—Embolisms in the upper limbs are generally better suited for conservative treatment with vasodilator agents, such as eupaverin, according to Denk, mainly because the collaterals are better preformed and thus there are better possibilities for an arterial supply of blood in the limb via other vessels than the one occluded. Conditions are far more unfavorable with reference to the lower limbs and the result of a conservative treatment is very doubtful, this having been demonstrated by a number of cases (Åkesson, Wiberg, Groth, and

others). I have discussed this question in another connection and refer to the paper in question.

A well-founded suspicion of a case being one of tumor embolism is of importance when determining whether the treatment is to be conservative or operative and considerably increases the misgivings about conservative therapy, especially in the case of embolism in the lower limbs. A piece of tumor that had been flung out would then be allowed to remain in the artery, possibly causing the development of a tumor in the limb.

Another matter worthy of special attention in this connection is the circulation in the limb in conjunction with embolism. There are reasons to presume that the extensive postembolic thrombosis starts as a coagulation of a blood column on the distal side of the embolus. If the embolus entirely occludes the artery and if, in addition, the collaterals are but little developed, the stoppage immediately causes a heavy drop in pressure on the distal side of the embolus, which results not only in a decrease in the caliber of the vessel, but also in the blood in the vessel being retarded, possibly stopped. (A spasm occurring, it may have a similar effect.) Due to the collaterals being different, this condition, which favors coagulation, is undoubtedly more decided in the lower limbs than in the upper. Other factors also influence the coagulation, special attention having been paid to the tendency of the blood itself, the coagulation differing from case to case. Lesions of the intima favor coagulation as the blood comes into direct contact with a tissue lacking endothelium. Similarly, it would appear probable that foreign tissues in the blood vessels, in this case tumor tissue, should favor coagulation.

There is good reason for assuming that subsequent to coagulation there is no flow of blood in the artery, even though the clot may not be of the normal caliber of the vessel. Owing to the drop in pressure in the artery after the stoppage, its wall will most probably be pressed against the clot. Merely as a result of the stoppage in the artery, causing the blood on the distal side of the embolus to be at a standstill or to move but slightly, but especially if postembolic thrombosis has started by the coagulation of that blood, the prospects of obtaining any kind of effect on the arteries by intravenous injections of eupaverin are thus nonexistent or in any case very small. The mouths of the collaterals are stopped and furthermore there is but little possibility for the eupaverin to advance in the arterial system of the obstructed limb. Eupaverin is an agent producing a direct effect on the smooth muscles in the vascular wall and has no remote effect conveyed by the nerves. Nor has intravenous treatment with eupaverin been established in any way to prevent secondary thrombosis (Åkesson) and the same appears to be true with reference to local intra-arterial injections, for in the case now described coagulation started

source was established. The case described above is thus of interest as the embolism undoubtedly emanated from the lungs.

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The clinical experience of heparinization in these operations is as yet very limited. A study of the recent literature, occasioned by the ease described above, disclosed that heparin has been used in a few cases of embolectomy in Toronto and at Örebro in Sweden. Murray and Best in 1938 gave a brief report on five cases, all of which passed off favorably. One of these cases was stated to be unfavorable from the outset and was not operated upon until after twenty-five hours. Judging from the information submitted, secondary thrombosis did not occur. The hemostasis caused no trouble. At the surgical congress in Berlin in 1939, Lindgren reported on three arterial operations in which heparin had been used. Two of his cases were embolectomies and the results were good. Secondary thrombosis does not seem to have occurred. In one of the cases the hemostasis caused trouble. In the case reported by me, the tendency to renewed thrombosis was very pronounced and thrombi were reformed after no less than four cleansings. Nevertheless, the effect was good after the fifth endeavor when heparin was used and there was no renewed coagulation, the circulation being restored. In this case the hemostasis caused no difficulties. This case, perhaps more than those mentioned above, promises increased possibilities of mastering the secondary thrombosis and improving the prognosis after embolectomy.

A few words may be added regarding the administration and dosing of the heparin and regarding the hemostasis. Incidentally, I must state that heparin retards the formation of thrombin but has no effect if coagulation has already occurred. This is its favorable effect which should be utilized. The dangers caused by the use of heparin in arterial operations are postoperative bleeding and greater difficulties in achieving hemostasis. This is the unfavorable effect of the agent, to be avoided or redneed. By administering the heparin at the right moment and in suitable doses, a successful result should be obtained with reference to these two respects.

As regards the right moment for heparinization, it is, of course, necessary to determine it according to the conditions in each special case. Olovson claimed that heparin fills its most important mission before the operation, when it is to prevent postembolic thrombosis, and he suggests preoperative injections of 100 to 150 mg. every other hour, to be started as soon as possible. In the operation described above, it appeared quite clear to me (postembolic thrombosis already existing) that the best effect of heparin ought to be obtained if the artery was first cleaned and closed, a regional injection then being made into the artery. Murray and Best as well as Lindgren adopted the same procedure. It would appear as if Olovson, when making his proposal, did not pay sufficient attention to the disadvantage of performing the operation after heparin had been administered. This is

afresh after such injections. Östling recently recorded a favorable effect of eupaverin injected into the artery after embolectomy and explains this by a condition of spasms immediately having been terminated. There appears to have been no postembolic thrombosis in his case.

Several reasons thus indicate that in cases of recently occluding large embolisms in the lower limbs vasodilator treatment should not be attempted, especially if there are reasons for suspecting tumor embolism. Operative treatment should be resorted to instead, first of all embolectomy. In the above described case it proved, however, that, in spite of the embolus' being removed together with a post-embolic thrombus covering practically the whole length of the limb and although intra-arterial injections of eupaverin were administered, the circulation did not start, due to a decided tendency to coagulation. A favorable result would certainly not have been attained unless an anticoagulant, heparin, had been available.

Heparin Treatment.—Heparin is a physiologic anticoagulant which is nontoxic in its present pure form. There is already a fairly extensive literature on its properties and its clinical and experimental use to date. In the April, 1939, issue of this JOURNAL Mason published a summary and recently Jorpes published a monograph on the subject (which appeared in Swedish as well as in English).

As regards our results after embolectomy when the embolus was difficult to reach (aorta aa. iliacae), I have previously published a paper in which I discussed the well-known fact that secondary thrombosis has an extremely unfavorable effect on the prognosis and hinted at the possibility of reducing it by the use of heparin. At that time there had been published no clinical experiences of heparinization in conjunction with vasosurgical operations. Pure heparin having become available, the experiences have been very favorable, especially in cases of postoperative thromboprophylaxis (Murray and Best, in Toronto; Crafoord, in Stockholm), as have been the experiences of vascular operations in animals. In this connection Murray and Best's experiments (1938) are of major interest. Upon performing experimental embolectomy in dogs twenty-four to seventy-two hours after sterile foreign bodies and pieces of thrombi had been placed in arterial bifurcations, postoperative thrombosis and negative results were recorded in all the nonheparinized cases; whereas, general or regional heparinization resulted in the circulation being restored after every embolectomy. In order to ascertain the risks of secondary hemorrhages, Olovson (1938-1939) performed arteriotomies, also in dogs, that were strongly heparinized, and was in all the cases able to arrest the bleeding without any great difficulties when the suture had been made.

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illustrated by one of Lindgren's cases. It was an aortic embolism with simultaneous embolisms in the two external iliac arteries, and arteriotomies were performed in three places, first in the aorta and then in the two femoral arteries. When the aortotomy had been sutured, a total of 90 mg. of heparin was injected in two doses with an interval of twenty minutes between injections. The aortotomy was then tight and remained so, but the process of arresting the hemorrhage after the sutures of the arteriotomies in the femoral arteries, which were performed after heparinization, was found to be very troublesome and revision was subsequently necessary due to bleeding. This would appear to be the only case of embolectomy in man hitherto made after heparinization.

It is certainly too early to draw any definite conclusions as to the best procedure, on the basis of the few cases so far published, but the experience gained, though it may, of course, partly be the result of accidents, would appear to supply certain hints as regards the administration that are worthy of attention. It is, of course, of extreme importance, from the very beginning, that this excellent and serviceable anticoagulant is not brought into disrepute owing to complications that possibly may be avoided. Doing a preoperative heparinization, however, we must take risks of considerable disadvantages (difficulty in hemostasis, afterbleeding). With this fact in mind, we ought to consider the obtainable advantages of this administration. In those late cases with a large postembolic thrombosis running out in the branches of the artery already occurred (Fig. 3), a preoperative heparinization is of no use, because the heparin cannot work in the blocked artery. It has been demonstrated that in a number of cases even a postembolic thrombus of considerable length has been pulled out and in my case that re-coagulation through postoperative heparinization may be avoided.

In early cases without or with only a slight postembolic thrombosis heparin may work favorably through collaterals, but, on the other hand, one or two hours' delay, before taking the patient to a hospital, seems to involve less risk than heparinization before the transport. Furthermore, it is not very likely that the general practitioner originally in charge of the case will have heparin available, and procuring it will mean a loss of valuable time. If the patient is in hospital and it has been decided that the operation shall be performed, the heparinization should be put off until the artery is free and the arteriotomy closed. This procedure would seem to me to be the least dangerous manner in which to utilize the favorable effect of heparin.

General rules for the dosing, based on sufficient clinical experiences, are as yet lacking. It goes without saying that the smallest effective dose must be the aim. In our case, 100 mg. injected intra-arterially

proved to be quite effective and entailed no complications. This dose corresponds to a little more than 1 mg. per kilogram of body weight. (The patient was a heavy person with considerable adipositas.) Lindgren recommends a more cautious dosing, $2/3$ mg. per kilogram of body weight. In one of his cases this dose produced a coagulation time of ten minutes, which remained after four hours and which he considers sufficient. The dosing during the subsequent course should, according to Lindgren, be determined from case to case, on the basis of repeated determinations of the coagulation time. Referring to their experimental examinations, Murray and Best consider that the risk for thrombosis ceases seventy-two hours after the operation. In my case it was found that a supply of 150 mg. per twenty-four hours, divided in three doses, was quite effective during the three days following the operation and caused no complications.

With reference, finally, to the difficulties in arresting the bleeding, Lindgren recommends a 0.5 per cent thionin solution, which is non-toxic. If swabs of cotton wool dampened in this solution and pressed against the bleeding spot do not produce the desired effect, it can be covered with a piece of muscle soaked in the solution, which heals and produces a reliable hemostasis. Intravenous injections of protamine are said completely to counteract the effect of heparin (Jorpes). However, the general effect of the heparin, which is desired, is, of course, also eliminated, and it is thus better if purely local hemostatic arrangements can be made.

SUMMARY

An uncommon case of embolectomy of the common femoral artery has been reported. It is remarkable, *inter alia*, in the following respects: The embolism emanated from a pulmonary vein. The embolus consisted mainly of a sarcoma. Together with the embolus there was extracted a postembolic thrombus, approximately 80 cm. long. Repeated arteriotomies and removals of re-formed clots and intra-arterial injections of eupaverin only produced temporary circulation, which was definitely restored when the artery had been cleaned out for the fifth time followed by an intra-arterial injection of heparin. The heparinization entailed no trouble. The source of the embolism and the treatment are discussed. Embolism in the lower limbs should be subjected to operative treatment, especially if tumor embolism is suspected. The limited clinical experience so far gained of heparinization in cases of embolectomy would seem to promise a better prognosis, there now being better prospects of mastering secondary thrombosis. Cautious heparinization should be performed after each embolectomy. The right moment for heparinization is when the artery has been cleaned and the incision sutured. Preoperative heparinization should be avoided as it entails unnecessary risks of complications.

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ANEURYSM OF THE SPLENIC ARTERY

LOUIS SPERLING, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota)

ANEURYSM of the splenic artery is rarely diagnosed during life. Schroeder recorded twenty cases in 32,768 post-mortem examinations (once in approximately 1,500 autopsies). In statistics of 41,437 autopsies summarized by Lindboe, there were 554 abdominal aneurysms, of which only 26 (0.05 per cent) were located in the splenic artery. Anderson and Gray collected fifty-eight cases in 1929 and presented a review of the symptomatology and literature. More recently Guy and also Seids and Hauser have reviewed the literature and added cases of their own. There are on record only eleven cases in which the patients have survived operation for this condition. Less than one hundred cases have been recorded since the report of Crisp in 1847.

In the Department of Pathology of the University of Minnesota, there are records of 33,810 autopsies to January, 1939. In this series, there were 393 aneurysms, seventy of which were located in the abdomen. Forty-eight involved the abdominal aorta; of these, twenty-six were ruptured. There were nine aneurysms of the iliac vessels, seven of the splenic artery, two each of the celiac and renal arteries, and one each involving the hepatic and superior mesenteric arteries. Six of the seven aneurysms involving the splenic artery were incidental findings at autopsy; and one had ruptured to cause death. All were described as arteriosclerotic in origin. Syphilis was not noted as an etiological factor in any of these cases.

Surgical removal of aneurysm of the splenic artery has been reported by Winekler, Mulley, Davis, Goulliod, Broekman, Lower and Farrell, Lindboe, and Parsons. According to Winekler, Selten was the first to operate upon one successfully. Marshall obtained a cure by proximal and distal ligation of the aneurysmal sac. Seids and Hauser (1940) reported another cure by ligation.

A correct preoperative diagnosis has been made in only three cases up to the present time. Höglér made the diagnosis on the basis of (1) left upper quadrant pain, (2) a systolic bruit over a palpable tumor mass, and (3) a pulsating filling defect in the greater curvature of the stomach. Lindboe made the correct preoperative diagnosis by means of the roentgenogram. He states that aneurysm of the splenic artery can be recognized by roentgen ray only when it is calcified. Seids and Hauser's case presented a palpable mass, a bruit, and, roentgenographically, a calcified area 9 cm. in diameter and medial to the spleen.

The case presented here exhibited the x-ray findings referred to by Lindboe as suggestive of aneurysm of the splenic artery, i.e., a calcified shadow situated in the left upper quadrant of the abdomen, overlying and projecting to the left of the twelfth thoracic vertebra.

Because of the rarity of the condition, and in the interest of more accurate preoperative diagnosis, it seems worth while to report in detail a case in which the possibility of aneurysm of the splenic artery was considered preoperatively. Recovery followed splenectomy and removal of the aneurysm.

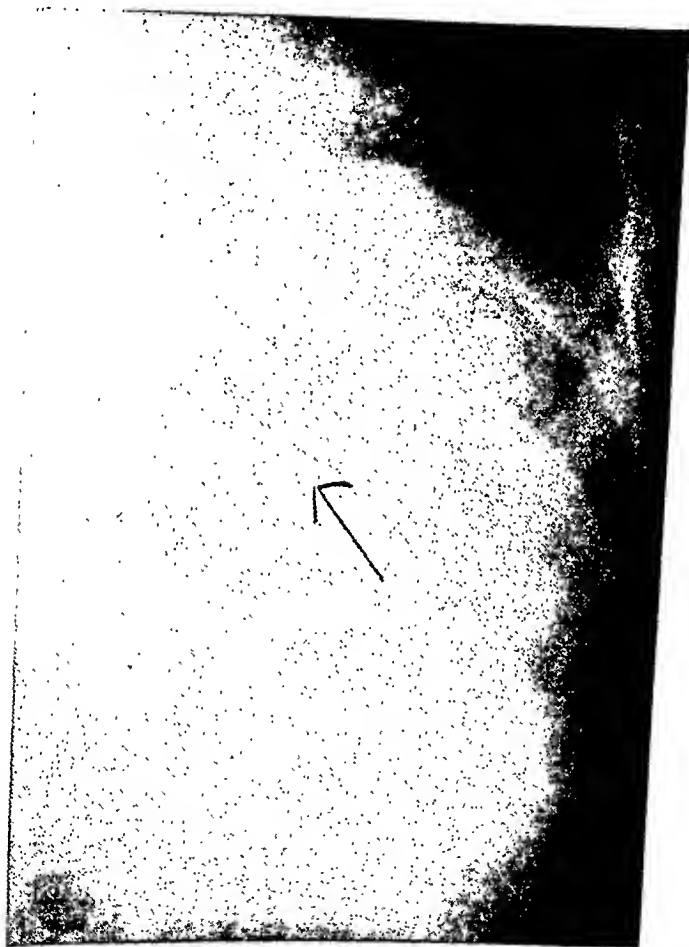


Fig. 1A.—Roentgenogram of the left upper quadrant of the abdomen, showing the shadow of a calcified aneurysm of the splenic artery.

CASE REPORT

Mrs. P. W., a married white female, 39 years old, University Hospital No. 661247, was admitted on Aug. 13, 1937, and discharged on Oct. 22, 1937.

Past History.—The patient had had cholecystectomy, appendectomy, and hemorrhoidectomy in 1932, and a right nephrectomy in 1933 for pyelonephritis and stone.

Since 1934 there had been repeated attacks of left pyelonephritis. Artificial menopause in 1935 followed radiation for menorrhagia.

Present History.—Since May, 1937, the patient had experienced recurrent attacks of severe colicky pain in the region of the upper end of the scar of the old cholecystectomy. This pain radiated to the right scapula. There had been anorexia and vomiting and alternating constipation and diarrhea. She had lost 40 pounds.

Examination revealed a blood pressure of 140/94. There was moderate tenderness over the upper end of the scar of the cholecystectomy and in the left flank. No masses were palpable in the abdomen, nor was a bruit to be heard. Rectal and proctoscopic examinations were negative. There was a scanty purulent bloody vaginal discharge. The uterus was situated anteriorly, freely movable, and slightly smaller than normal. There were no adnexal masses.



Fig. 1B.—Roentgenogram of the left upper quadrant of the abdomen after operation; the shadow is no longer present.

The catheterized urine contained a heavy cloud of albumin and a few granular casts and was sterile. The hemoglobin was 98 per cent, and the white blood count and differential were normal. The Wassermann reaction was negative. The stools contained neither occult blood nor parasites; the icterus index was 11. Gastric analysis showed no free acid. Material aspirated from the duodenum following the administration of magnesium sulfate did not reveal any cholesterol crystals. The

phenolsulphonephthalein excretion was 46 per cent in two hours; the sedimentation rate was normal. Skin tests for echinococcosis were negative.

There was some disturbance of glucose tolerance as evidenced by the following blood sugar values after a test meal: at thirty minutes, 124 mg.; at one hour, 204 mg.; at two hours, 165 mg.

Roentgenologic study of the gastrointestinal tract was entirely negative. There was a dense shadow just to the left of the spine at the level of the twelfth dorsal vertebra. The exact nature of this density was not determined by the roentgenologist, who suggested the possibility of a calcified cyst (echinococcus) in the left lobe of the liver or an atypical calculus in the tail of the pancreas. The dense shadow was found to be behind the stomach and above the left adrenal and kidney. Excretory urograms revealed a normal left renal pelvis, ureter, and bladder.



Fig. 2.—Gross specimen of the excised spleen and calcified aneurysm of the splenic artery.

Because of the disturbance of the glucose tolerance and the location of the calcification, the diagnosis of a calcified pancreatic cyst was suggested by the medical consultant. The urologic consultant thought that the pain was unrelated to the urinary tract. The possibility of a calcified aneurysm of the splenic artery was suggested by Dr. O. H. Wangenstein on the basis of the roentgenologic findings.

The pain was definitely relieved by the administration of nitroglycerin and temporarily relieved by infiltration of the abdominal wall with procain. The patient's condition grew worse because of continued vomiting, and on Sept. 23, 1937, the abdomen was explored by Dr. O. H. Wangenstein.

Operative Findings.—"When the abdomen was opened, there were dense adhesions from the omentum to the entire right abdominal wall anteriorly and laterally. The common duct was retracted somewhat medially, but was normal in size and consistency. The ovaries were pea-sized on both sides. The pelvis was otherwise negative. There was a large pulsating mass in the hilum of the spleen."

Operative Procedure.—"When the stomach had been separated from the upper pole of the spleen, a large dense mass was found intimately related to the splenic artery and medial surface of the spleen. The gastrosplenic omentum and the lienorenal and vascular ligaments were divided, and the spleen was delivered into the wound. It was evident that the hard mass was part of the splenic artery. The latter was clamped proximal to the mass, which was then removed with the spleen. The patient stood the operative procedure nicely."

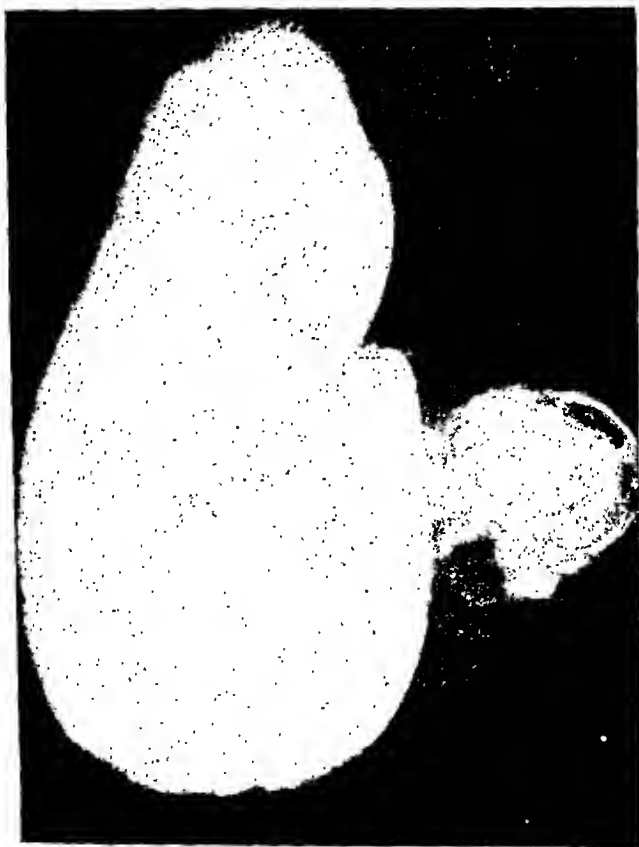


Fig. 3.—Roentgenogram of the excised specimen.

Pathologic Report.—"The spleen itself is approximately normal in size. The splenic artery has been cut about 4 cm. from its bifurcation, at which there is an aneurysm measuring 2 cm. in diameter. The aneurysm projects from the surface of the artery as the closed end of a U, and its walls are thin, slightly lobulated on the internal surface, and heavily infiltrated with calcareous material. On one of the branches of the splenic artery beyond the bifurcation there is a similar but smaller aneurysm measuring about 5 mm. in diameter and about 1 cm. in length. The aneurysm was not dissected but was preserved for a museum specimen."

Conclusion.—Arteriosclerotic aneurysm of the splenic artery.

The patient had an uneventful convalescence from her operation and was discharged from the hospital on Oct. 22, 1937. In August, 1938, the patient had no complaints.

SUMMARY

A calcified aneurysm of the splenic artery is reported. The classical roentgenologic picture described by Lindboe was present and led to a correct preoperative diagnosis. The aneurysm was excised, together with the spleen, and the patient made an uneventful recovery. This is the twelfth recorded instance in which the patient recovered from operation for aneurysm of the splenic artery. Seven additional cases recorded in the autopsy material (33,810 autopsies) of the Department of Pathology of the University of Minnesota are added to those previously reported in the literature.

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CAVERNOUS HEMANGIOMA OF THE SPLEEN

FRANK L. COLE, M.D.,* AND JAMES H. FORSEE, M.D.,†
WASHINGTON, D. C.

(From the Surgical Service, Walter Reed General Hospital)

CAVERNOUS hemangioma of the spleen is an uncommon disease. The rupture of a cavernous hemangiomatous spleen successfully treated by emergency splenectomy has not been reported previously as far as we have been able to ascertain. In 1938, Akcakoyunlu reported a collected series, including one of his own, of twenty-one cases of benign hemangioma of the spleen, and in only one was there an emergency due to rupture of the spleen.¹ In 1933, Haines and McIlroy reported the single case of spontaneous rupture of the spleen.² Their patient was a white married woman 43 years of age, who, twenty-four hours prior to hospital admission and unassociated with trauma, was seized with extremely severe pain in the epigastrium. Nausea and vomiting soon followed. The pain was localized chiefly in the epigastrium, but was present to a moderate degree in the right lower quadrant. Physical examination disclosed the patient to be semicomatose and gasping for air, "the entire abdomen was tender, exquisitely tender in the epigastrium and moderately tender in both upper quadrants."² A tentative diagnosis of an acute perforation of a gastric ulcer was made and immediate operation was performed. The peritoneal cavity contained a large quantity of bright red blood; the spleen was surrounded by fresh adhesions, and the organ was removed. Near the upper pole of the spleen a collection of cystlike spaces containing blood was present, and the largest of these had ruptured. Death occurred forty-eight hours after the operation. In the case to be reported, splenectomy was performed seventeen hours after the onset of symptoms.

Hemangioma of the spleen is a primary vascular tumor and may be either capillary or cavernous. In the former there is a formation of dilated vascular channels in the splenic tissue which gradually become converted into tubules. In the cavernous type the capillary system is lost, and the hemangioma consists of a series of freely intercommunicating spaces of varied sizes, lined with endothelium. Ordinarily, they are considered congenital. The published case reports are confusing in that several are described as malignant neoplasms metastasizing to adjoining organs, especially the liver. This is true in the cases reported by Langhans (1879),³ Homans (1897),⁴ Theile (1904),⁵ Wright (1928),⁶ and

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*Lieutenant Colonel, Medical Corps, U. S. Army.

†Captain, Medical Corps, U. S. Army.

Dowd (1915).⁷ In 1895, Hodge stated, "Apparently all gradations occur from single localized or widely diffuse telangiectatic changes to more or less encapsulated angiomatic nodules, and finally to highly malignant tumors with metastasis."⁸ Abrams recently has reported a most interesting case of a "histologically benign metastasizing hemangioma involving spleen, liver, kidneys, pancreas, adrenals, intima of the pulmonary artery, the right lung, and the mesenteric, peripancreatic, pre-aortic, and mediastinal lymph nodes."⁹ Matas described the behavior of angiomas of the spleen as characteristic of that of a benign neoplasm.¹⁰

The benign hemangiomatic spleen may reach an enormous size. Akeakoyunlu reported a case treated by splenectomy, with recovery, in which the spleen weighed 7,240 Gm.¹ Zeno and Cid report recovery following splenectomy of an angiomatic spleen weighing 5,800 Gm.¹¹ Steden reported a similar case in which the spleen weighed 4,812 Gm.¹² Ordinarily, the involved spleen is much smaller. The reported cases demonstrate that there is great variance in age, the youngest patient being 4 months and the oldest, 65 years. Usually the symptoms are of several months' or years' duration and are characterized by a gradually increasing tumefaction in the left hypochondrium, associated with pain, loss of weight, and anemia. Thus, ample time is available for a thorough clinical study prior to operation. Surgery is the only curative therapy, and splenectomy is necessary.

The reported cases of benign hemangioma of the spleen are tabulated in Table I. A total of twenty-two cases has been reported previously. We wish to add a case report to this list. Schottenfeld and Wolfson state that the records of the Jewish Hospital, Brooklyn, show that four additional cases of small splenic hemangiomas were discovered at necropsy which had not given symptoms during life, but data on these cases are not furnished.¹³

CASE REPORT

An army officer, white, aged 27 years, was admitted to the Walter Reed General Hospital on May 1, 1939, complaining of the sudden onset of moderate intermittent cramplike pain in the upper abdomen thirteen hours prior to admission. Within one hour after the onset he drove his automobile twenty-two miles, but the trip was temporarily interrupted because of vomiting and increased pain. He slept intermittently from 1:00 to 5:30 A.M., and by that time the pain was violent, although it remained cramplike in character, being increased by deep respirations and on turning from side to side. There was no further vomiting. The pain continued and was localized chiefly across the upper abdomen, but it involved the entire abdomen. Previous significant history included an acute attack of severe pain in the left upper abdomen and back on Sept. 13, 1938, which subsided rapidly without clinical investigation. On March 27, 1939, the patient was thrown from a horse and suffered slight pain in the left hypochondrium and beneath the corresponding lower ribs. He was able to ride horseback the following day and continued his work uninterruptedly.

On physical examination, the patient was rational, lying quietly in bed, and in apparent pain. The temperature was 98° F.; pulse, 80; respiration, 20; and blood pressure, 140/80. The abdomen was distended slightly and was moderately tender

TABLE I*
COLLECTED CASE REPORTS OF BENIGN HEMANGIOMA OF THE SPLEEN

| AUTHOR | SEX | AGE | DURATION | SYMPTOMS | OPERATION | RESULT | DIAGNOSIS |
|--------------------------------|-----|-------|------------|--|-------------|---------------------|---|
| | | | | | | | |
| Hodge, Jr. | F | 43 | 4 yr. | Abdominal mass; constipation; diarrhea; loss of weight | Splenectomy | Cured | Cavernous hemangioma |
| Martin and Ombredanne | F | 31 | Months | Pain; abdominal mass; constipation; loss of weight | Splenectomy | Cured | Angioma |
| Albrecht | M | 65 | - | Autopsy report | - | - | Cavernous hemangioma |
| Thiele | M | 22 | - | Autopsy report | - | - | Obliterating angioma |
| | M | 36 | - | Autopsy report | - | - | Obliterating angioma |
| | M | 62 | - | Autopsy report | - | - | Cavernous hemangioma |
| V. Benkendorf | M | 53 | 2 yr. | Abdominal mass | Splenectomy | Not reported | Cavernous hemangioma |
| Angiotti | F | 38 | 14 mo. | Pain; vomiting | Splenectomy | Cured | Capillary angioma |
| Muller | M | 30 | - | Autopsy report | - | - | Cavernous hemangioma |
| Steden | M | 42 | 8 yr. | Abdominal swelling, left | Splenectomy | Cured | Cavernous hemangioma |
| Orlandi | F | 44 | 1 yr. | Fatigue; edema of extremities | Splenectomy | Died 3 hours later | Cavernous hemangioma |
| Schwarz | F | 35 | 4 mo. | Pain; abdominal swelling, left upper quadrant | Splenectomy | Cured | Cavernous hemangioma |
| Zero and Cid | M | 30 | 5 mo. | Loss of weight; abdominal mass; fatigue | Splenectomy | Cured | Hemangioma endotheliona |
| Wasiljeff and Pratussewitch | M | 32 | 1 mo. | Swelling, left hypochondrium | Splenectomy | Cured | Capillary hemangioma |
| Keller | F | 52 | - | Abdominal mass; chill; fever | Splenectomy | Cured | Cavernous hemangioma |
| Palveino, Village, and Palazon | M | 41 | 20 yr. | Abdominal swelling | Splenectomy | Cured | Angiomatosis |
| Haines and McIlroy | F | 43 | - | Sudden severe epigastric pain; nausea; vomiting | Splenectomy | Died 48 hours later | Spontaneous rupture of cavernous hemangioma |
| Grove | F | 4 mo. | Congenital | Abdominal mass; vomiting; constipation | Splenectomy | Cured | Fibromangioma |
| Milani | F | 45 | - | Autopsy report | - | - | Cavernous hemangioma |
| Akcaoyunlu | M | 30 | 3 yr. | Abdominal mass; dyspnea | Splenectomy | Cured | Capillary and cavernous hemangioma |
| Schottenfeld and Wolfson | F | 31 | 7 yr. | Abdominal mass | Splenectomy | Cured | Cavernous hemangioma |
| Naher | F | 42 | 5 yr. | Enlargement of abdomen | Splenectomy | Died 30 days later | Hemangioma |
| Cole and Forsee | M | 27 | 17 hr. | Sudden epigastric pain | Splenectomy | Cured | Rupture of cavernous hemangioma |

*Condensed from Akcaoyunlu, with additional case reported by Schottenfeld and Wolfson and the authors' case. See references 1 and 13.

throughout, but with most marked tenderness in the right lower quadrant. The blood picture was as follows: erythrocytes, 4,400,000; hemoglobin, 80 per cent; leucocytes, 15,200, and polymorphonuclears, 84 per cent; coagulation time, $2\frac{1}{2}$ minutes, and bleeding time, $2\frac{1}{4}$ minutes. The urine analysis was negative. A tentative diagnosis of acute appendicitis was made, and immediate operation was performed. The peritoneum was opened through a McBurney's incision, and blood welled into the wound. Appendectomy was performed although the organ appeared normal. The

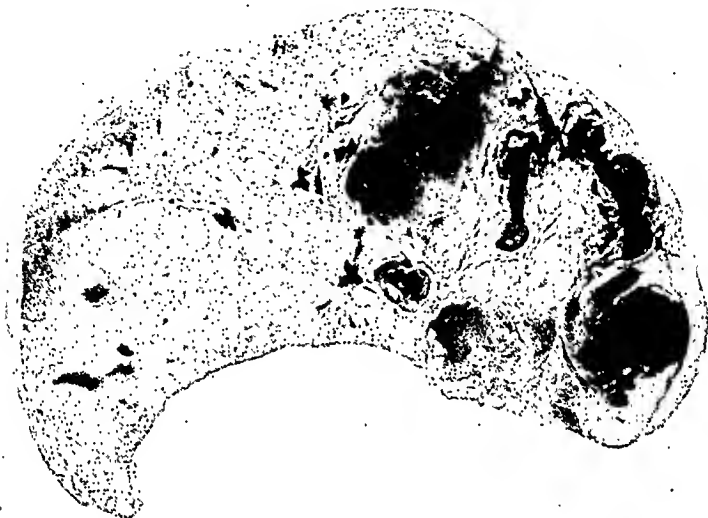


Fig. 1.—Section of spleen showing the cavernous hemangioma. Adherent clot was present over the surface of the angiomatous space on the concave surface. There is a recent rupture on the right side of the convex surface about midway from bottom to top of the illustration. (U. S. Army Medical Museum, Neg. No. 68675.)

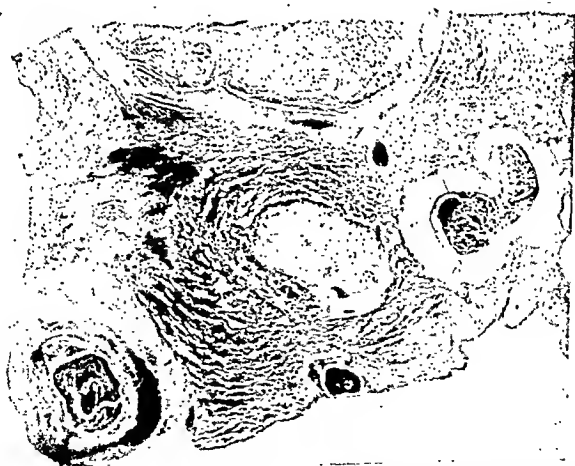


Fig. 2.—Low-power photomicrograph of section through several of the angiomatous spaces, showing thick fibrous walls and somewhat retracted blood clots in the lumina. Note hemorrhage into tissues at left center. (U. S. Army Medical Museum, Neg. No. 68763.)

McBurney's incision was closed, and a 15 cm. midline upper abdominal incision was made. A large quantity of free blood was evacuated from the peritoneal cavity, and the liver, stomach, and duodenum were found to be normal. On palpation, the spleen was found to have an area at its lower pole which had ruptured, and splenectomy was performed. The postoperative course was uneventful, and the patient left the hospital twenty-three days after operation. Seven months later he was in perfect health.

Pathologic Report. Gross Findings.*—The specimen (Fig. 1) is a spleen weighing 225 gm., preserved in formalin solution. The lower pole, about one-third of the spleen structure, is composed of multiple more or less spherical nodules, from 0.5 to 3.0 cm. in diameter, filled with dark, formalin-fixed blood. There is a lacerated wound 1.5 cm. long and 0.4 cm. wide on the external surface, about 3 cm. from the margin. There is no reaction about this wound. On the inner surface of the lower pole there is an open lacerated area, 3 cm. in length by about 1.5 cm. in diameter, covered with an adherent dark clot. The rest of the splenic tissue appears essentially normal.

Microexamination.—Sections from the main splenic tissue are essentially normal (Fig. 2). Sections from the lobulated areas show them to be composed of dense fibrous walls lined in occasional areas with endothelium. Most of the lobules, however, show fairly recent clot beginning to undergo organization by fibroblastic proliferation from the wall.

The diagnosis was cavernous hemangioma of the spleen with rupture of part of the tumor.

SUMMARY

A case of ruptured cavernous hemangioma of the spleen, mistakenly diagnosed as acute appendicitis, which was successfully treated by splenectomy is recorded. No similar case report in which the patient recovered has been found in the literature. The recorded cases of benign hemangioma of the spleen have been tabulated and brought up to date, the list containing twenty-three cases.

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*G. R. Callender, Colonel, Medical Corps, U. S. Army.

FURTHER STUDIES OF HEMORRHAGE AND SERUM INFUSION

F. NEUWELT, M.D., S. O. LEVINSON, M.D., WILLIAM OLSON, AND
H. NECHELES, M.D., PH.D., CHICAGO, ILL.

(From the Department of Gastro-Intestinal Research and the Samuel Deutsch Serum Center of Michael Reese Hospital)

IN A previous paper¹ we demonstrated that severe shock from hemorrhage requires prompt restoration of circulating fluid volume and that immediate restitution of red blood cells is of only secondary importance in most cases. We were able to demonstrate that serum is a good substitute for whole blood and pointed out that it has certain advantages which make it more useful and practical than blood. Sterile pooled serum can be kept ready for immediate use for long periods of time² and may be infused in large amounts without preliminary typing or compatibility tests.

In the experiments reported in our previous paper we transfused dogs following hemorrhage with amounts of blood, serum, saline or glucose solution equal to the total amount of blood lost by bleeding. For very practical reasons we were interested in finding out experimentally whether infusion with amounts of serum smaller than the volume of blood lost in hemorrhage would give satisfactory results in combatting shock and how such infusions of serum would compare with infusions of whole blood. Johnson and Blalock³ showed that in dogs the removal of whole blood is tolerated better than the loss either of blood plasma or of red cells.

Experimental Procedure.—This has been described in detail previously¹ and is only briefly recapitulated here. Under light ether anesthesia the right carotid artery and jugular vein were isolated and cannulated aseptically. Three hours were permitted to elapse to allow the animal to recover from the effects of anesthesia. Blood pressure, pulse, respiration and temperature, red blood cell count, hemoglobin, hematocrit, blood CO₂, O₂, N.P.N., plasma proteins and chlorides were determined before every bleeding. Certain of the above determinations were repeated at more frequent intervals. Blood pressure was measured with a tyco anaeroid gage connected to the carotid artery. The animals were infused through the jugular vein at a uniform rate of 20 c.c. per minute with their own citrated blood removed at the preceding bleeding or with the serum of other dogs. Compatibility tests were done and only compatible serum used.⁴ At the termination of each experiment, the cannulae were removed, the wounds dressed, and the animal returned to its cage.

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Bleeding was performed at a uniform rate of 25 c.c. per minute. Thirty per cent of the calculated circulating blood volume* was removed and thirty minutes later blood or serum was administered. One-half hour later the next bleeding took place. This procedure was repeated until the animal had been bled of 80 per cent of the calculated circulating blood volume in successive stages of 30, 20, 20, and 10 per cent. In those dogs reinfused with serum the actual cell volume removed was only 66.6 per cent, due to progressive dilution of the blood by the serum infusions. The amount of blood or serum reinfused was equivalent only to the plasma volume removed at the preceding bleeding; thus the decrease in volume from loss of the cellular elements was not restored. Furthermore, there was no restitution of the blood removed for chemical determinations, etc., totaling 125 to 175 c.c. in each experiment.

Results.—Sixteen experiments were performed, eight dogs receiving their own citrated whole blood and eight others receiving dog serum. The results are summarized in Table I.

TABLE I

| | NO. OF EXPERI- MENTS | SURVI- VAL | AVERAGE BLOOD PRESSURE | | AVERAGE BLOOD CHEMICAL DETERMINATIONS | | | | REMARKS |
|------------------------------------|----------------------------|---------------|---------------------------|-------|--|-----|----------|---------|---|
| | | | | | INITIAL | | | | |
| | | | | | FINAL | | | | |
| | | | INITIAL | FINAL | CO ₂ | CL. | N. P. N. | PROTEIN | |
| Serum-in- fused dogs | 8 | 6 | 153 | 111 | 37.3 | 606 | 29 | 6.2 | As judged by clinical con- dition, the surviving serum- infused dogs were in some- what better physical status than the surviving whole blood- infused dogs |
| | | | 99 | 71 | 36.1 | 623 | 29 | 5.9 | |
| Whole blood- infused dogs | 8 | 7 | 149 | 102 | 36.1 | 654 | 28 | 5.8 | |
| | | | 96 | 75 | 32.4 | 662 | 29 | 4.9 | |

Dogs reinfused with blood received an average of 60 per cent of the total blood removed (54 to 74 per cent). Dogs reinfused with serum received an average of 68 per cent of the volume of blood removed by hemorrhage (64 to 71 per cent). The latter group† received more fluid in reinfusions than did the former because in the successive bleedings and reinfusions with serum the proportion of serum to corpuscular elements increased.

One blood dog and two serum dogs died during the course of the experiments. This contrasts unfavorably with results reported in our first paper in which complete volume restoration was done and in which

The literature contains values for blood volume of dogs which vary from 7.5 to 11 per cent of body weight. We arbitrarily chose the figure of 7.5 per cent of body weight as representing the circulating blood volume of the dog.

†For brevity dogs infused with blood or serum are designated as blood dogs or serum dogs respectively.

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F. NEUWELT, M.D., S. O. LEVINSON, M.D., WILLIAM OLSON, AND
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¹Received for publication, January 23, 1940.

and protein values than the animals presented in this paper. We must attribute part of the drop of blood pressure in all the experiments to the long duration of these experiments. The dogs in our previous experiments were in better physical condition at the end of the experiment than those presented in the present paper.

TABLE II

| INFUSION WITH | NO. OF EXPERIMENTS | SURVIVAL | AVERAGE BLOOD PRESSURE | | AVERAGE BLOOD CHEMICAL DETERMINATIONS | |
|---------------|--------------------|----------|------------------------|-------|---------------------------------------|---------|
| | | | | | INITIAL | |
| | | | | | FINAL | |
| | | | INITIAL | FINAL | CO ₂ | PROTEIN |
| Serum | 12 | 12 | 158 | 128 | 39.0 | 6.6 |
| | | | 105 | 77 | 38.5 | 6.4 |
| Blood | 5 | 5 | 178 | 137 | 36.9 | 6.2 |
| | | | 108 | 97 | 34.3 | 5.3 |

SUMMARY AND CONCLUSIONS

Successive hemorrhages in dogs and only partial restoration with serum or blood does not permit survival of all animals, while reinfusion with amounts of serum or blood equal to the total volume of blood lost preserved the life of the animal in each instance. Our experiments show that serum and blood are of nearly equal value when transfusing amounts smaller than those lost in graded massive hemorrhages. In shock from massive hemorrhage maximal rather than minimal amounts of serum or blood should be administered.

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all animals survived. Both groups of animals showed comparable falls in blood pressure during the course of the experiments, and the final blood pressure readings one-half hour after the fourth infusion disclosed that the serum group had an average blood pressure value of 111/71 compared with a value of 102/75 for the whole blood-infused dogs.

The chemical determinations revealed a small drop in the alkali reserve and a decrease in the plasma protein value of the blood dogs. The latter decrease cannot be due to diluting effects of citrate because a concentrated solution was employed as anticoagulant. It may be due to the fact explained above that the blood dogs received less total reinfusion than did the serum dogs.

Erythrocyte count, hemoglobin and hematocrit values dropped 10 to 20 per cent in the blood dogs and 40 to 60 per cent in the serum dogs. The pulse rate was increased in both groups of dogs, being somewhat higher in the serum dogs than in the blood dogs.

DISCUSSION

Our data show that reinfusion with amounts of blood or serum smaller than that lost by hemorrhage did not save the life of all animals, while in previous work reinfusion with amounts of blood or serum equal to that lost kept all animals alive. There are no accurate or rapid methods of determining the amount of blood lost in massive continuous or repeated hemorrhage in human beings. Since incomplete restoration of volume by either blood or serum is not as effective or as lifesaving as complete restoration, it would seem advisable that maximal rather than minimal quantities of serum or blood should be administered. We must take into consideration the arguments against infusion in conditions like bleeding ulcer where infusion which sustains the blood pressure may also counteract spontaneous cessation of hemorrhage. It is not our purpose here to enter into a discussion of the pros and cons of infusion in such circumstances, but it should be pointed out that, if the hemorrhage has been excessive, a fatal outcome from shock is probable and it must be combatted by transfusion to maintain an adequate circulating blood volume. Furthermore, our results indicate that serum infusion seems to be as beneficial as whole blood even if there is only partial replacement of volume following graded massive hemorrhage. The anemia produced in the serum dogs as noted previously caused no distress and the animals showed no evidence of anoxia or acidosis. The general physical condition of the serum dogs surviving the experiments seemed slightly better than that of the blood dogs, possibly due to the fact that they had received a somewhat larger amount of fluid.

Table II, presented for contrast, shows the results obtained in our previous work¹ in which amounts of blood or serum equal to the total volume of blood (plasma plus cells) lost in hemorrhage were reinfused. These animals had a higher final blood pressure and slightly better CO₂

and protein values than the animals presented in this paper. We must attribute part of the drop of blood pressure in all the experiments to the long duration of these experiments. The dogs in our previous experiments were in better physical condition at the end of the experiment than those presented in the present paper.

TABLE II

| INFUSION WITH | NO. OF EXPERIMENTS | SURVIVAL | AVERAGE BLOOD PRESSURE | | AVERAGE BLOOD CHEMICAL DETERMINATIONS | |
|---------------|--------------------|----------|------------------------|-------|---------------------------------------|---------|
| | | | | | INITIAL | |
| | | | INITIAL | FINAL | CO ₂ | PROTEIN |
| Serum | 12 | 12 | 158 | 128 | 39.0 | 6.6 |
| | | | 105 | 77 | 38.5 | 6.4 |
| Blood | 5 | 5 | 178 | 137 | 36.9 | 6.2 |
| | | | 108 | 97 | 34.3 | 5.3 |

SUMMARY AND CONCLUSIONS

Successive hemorrhages in dogs and only partial restoration with serum or blood does not permit survival of all animals, while reinfusion with amounts of serum or blood equal to the total volume of blood lost preserved the life of the animal in each instance. Our experiments show that serum and blood are of nearly equal value when transfusing amounts smaller than those lost in graded massive hemorrhages. In shock from massive hemorrhage maximal rather than minimal amounts of serum or blood should be administered.

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SUBDIAPHRAGMATIC (PERIRENAL) EXTENSION OF STAPHYLOCOCCIC EMPYEMA

VERNON A. WEINSTEIN, M.D., NEW YORK, N. Y.

(From the Surgical Service of Dr. Harold Neuhof, Mt. Sinai Hospital)

TRANSDIAPHRAGMATIC and retrodiaphragmatic extension of infections comprise a subject of considerable interest. There are numerous accounts of infections beginning beneath the diaphragm either in the intraperitoneal spaces or in the perinephric region which have traversed the diaphragmatic barrier and induced pleural and pulmonary complications. Ochsner and DeBakey,¹ in a comprehensive review of the subject of subphrenic abscess, found that 63 per cent of their cases had pleural or pulmonary complications. Hoehberg² stated that 85 per cent of 111 cases of subphrenic abscess presented thoracic complications, and that in 45 per cent of these the symptoms at the onset were referable to the thorax. Nesbit and Keene³ reported a series of cases of perinephric abscess which perforated into the bronchial tree. Beye⁴ recorded 31 cases of subphrenic (intraperitoneal) infection of which 23 had thoracic complications, and also 8 cases of perinephric abscess with similar complications. On the other hand, his review of a series of 337 cases of empyema revealed only 1 in which a subphrenic abscess was caused by extension of the infection from the pleura, and in that case the diaphragm was injured at the time of operation. Beye's conclusion is that the diaphragm is an efficient barrier against extension of infection from the thorax to the abdomen.

The evidence therefore points to the rarity of invasion of the subphrenic space by an empyema. It is interesting to note that Osler,⁵ in his discussion of empyema and perforation of the diaphragm, states that it is often difficult to tell on which side of the diaphragm the infection begins. He cites the presence of peritonitis, either general or local, in 9 of 38 autopsies on cases of empyema. He adds: "An abdominal abscess, starting from the pleura, may perforate the stomach, the intestines, or the kidney. It may extend along the spine to the iliac fossa and simulate a psoas or lumbar abscess."

The possible subphrenic pathways were surveyed by Lillienthal.⁶ He states that a chronic empyema "may invade any of the contiguous body spaces by perforating directly through structures bounding those spaces, notably the diaphragm. It may perforate into the hollow viscera of the abdomen, the stomach and intestines, the liver, etc."

There are a number of specific instances of the above which have been reported and can be briefly reviewed. Deane⁷ describes a case of empyema necessitatis which pointed in the loin. Dyson⁸ placed on record a

case of empyema with diaphragmatic perforation and gastrophrenic fistula, in which the possibility of operative injury to the diaphragm was admitted but was considered unlikely. Harzbecker⁹ reported a case of empyema in a patient with a long history of cough and expectoration. Following drainage of the empyema, a large perinephric abscess extending up to the eleventh rib on the same side was discovered. Since no direct communication was demonstrable between the perinephric abscess and the already healing empyema, Harzbecker considered the perinephric abscess to be metastatic from the original bronchiectasis. Tees¹⁰ reported a case in which a lumbar abscess could be traced directly to an acute infrapulmonary empyema. He also mentions a similar case report by Fagge and Smith. Swan,¹¹ in his review of 114 cases of subphrenic abscess, cites one case in which the infection was of pleural origin.

The following is the report of a case which apparently belongs to the group of pleural infections which have penetrated or extended behind the diaphragm to involve subdiaphragmatic structures. The chief purpose in reporting this interesting case is to survey the pathways of extension across the diaphragm.

CASE REPORT

The patient was a 48-year-old housewife, complaining of right loin pain, fever, and weakness. Her past history included an appendectomy and a right salpingo-oophorectomy twenty-two years before, a right pleurisy seventeen years before, and osteoarthritis sixteen years prior to her present admission. One year ago she had severe pain in her back on the right side which incapacitated her for several days. Ten weeks prior to the onset of the present illness, there were a number of furuncles and small carbuncles about the neck and axillae, the last of which healed a few weeks before this illness began. During this time several badly infected teeth were removed and a moderately severe gingival infection was treated.

The present illness began seven weeks before admission to the hospital, with chills and pain in the right lower chest. Signs of consolidation appeared over the right lower lobe. For several days she ran a course typical of lobar pneumonia with chest pain, tachypnea, fever, and slight cyanosis. The diagnosis was made by her physician and confirmed by consultants. Cough was minimal, and the sputum scanty, colorless, odorless, and tenaceous. Pneumococcus type XI was recovered from the sputum by mouse typing on two occasions. By the fifth day the signs over the right lower lobe had changed from dullness and bronchial breathing to flatness and diminished breath sounds. There was some amelioration of symptoms on the seventh day, but the temperature rose again that night. From that time on fever ranged between 101 and 104°. Tachypnea was persistent. Two thoracenteses were done. Seventy-five cubic centimeters of fluid, containing few white cells and no organisms, were obtained the first time. No fluid was obtained on the second tap. The chest signs were quite constantly dullness to flatness, diminished breath sounds, and a few rales at the right base. Two roentgenograms were taken. The first, after three weeks, showed some elevation of the right diaphragm and cloudiness in the right cardiophrenic angle and interlobar fissure. The second, taken after five weeks, revealed some resolution of the cloudiness, but the diaphragm remained elevated. About one and one-half weeks prior to admission, pain in the right flank appeared and became progressively more severe up to the time of admission.

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the parietal and viscerai pleura, thus sealing off the infection from the general pleural cavity. Neuhoof and Berek,¹³ in their studies of staphylococcus empyema, describe this type of lesion in adults. They state that in these patients the pleural reaction tends to be that of a sacculated empyema or pyopneumothorax in contradistinction to the subtotal or total empyema or pyopneumothorax as found in children where firm pleural adhesions fail to form early.

Given then a sacculated empyema, the next phase was perforation of the parietal pleura, peripleural extension, and invasion of the diaphragm or dissection behind that structure. The appearance of loin pain on about the fortieth day was apparently the signal of spread of the infection downward. The consideration of the pathways along which such a spread might take place is a matter of clinical as well as anatomical interest.

Obviously a suppurative process on one side of the diaphragm may reach structures on the other side by direct spread in only one of two ways, either by penetrating that organ or skirting its attachments. Direct invasion through the diaphragm occurs at first via the lymphatics, and later, with more severe infection, gross invasion of the musculature takes place with actual perforation.⁴ The normal lymphatic drainage in this region is directed upward, which is one of the factors accounting for the frequency of thoracic complications following subphrenic infection. Given, however, a suppurative process in the chest with blocked lymphatics above the diaphragm, retrograde lymphatic drainage from above downward can occur.²

Potential avenues of communication between the thorax and the abdomen are present in the connective tissue about the various structures that traverse the diaphragm. For example, the space between the aorta and the diaphragmatic crura is filled with loose areolar tissue continuous with the mediastinum above and the retroperitoneal tissues below. Pathways exist for the spread of infection along the course of other structures, such as the superior epigastric artery passing between the costal and sternal diaphragmatic attachments, the musculophrenic artery between its attachments to the seventh and eighth ribs, the vena cava, and the esophagus.¹⁴

Instead of penetrating the diaphragm, an infection may spread around its attachments. The possible anatomical pathways are of interest and in the past have received scant attention. Posteriorly the pathway might be behind the medial or lateral lumbocostal arches from which the diaphragm takes origin. The lumbocostal arches are fibrous thickenings in the sheaths of the psoas and quadratus lumborum muscles. These muscles arise at a higher level than their arches and, as a result, an infection perforating the parietal pleura in this area comes directly into contact with one of these muscles and may follow the muscle down behind the lumbocostal arches and the muscle sheaths into the lumbar

Physical examination revealed a pale, acutely ill woman. Temperature was 102.6°; respiration, 30; pulse, 112. There was dullness to flatness at the right base with diminished breath sounds over that area. There was extreme tenderness in the right costovertebral angle. The fingers were not clubbed; the abdomen was negative. W.B.C., 16,600 with 84 per cent P.M.N.; 15 per cent lymphocytes and 1 per cent mononuclears; Hg., 48 per cent; urine contained only a few white cells. Chest x-ray revealed a dense shadow in the right lower chest which was interpreted as fluid dipping beneath the base of the lung. The portion of the right lung that was visualized and the entire left lung showed no abnormalities.

The chest was aspirated in the right eighth intercostal space and a small amount of pus was obtained.

Operation was performed under avertin-nitrous oxide-oxygen anesthesia. An incision was made over the ninth rib below the angle of the scapula and that portion of the rib excised. The pleura posteriorly seemed inflamed. Several aspirations were made at this time; some bloody fluid was obtained; but pus was not encountered. A cautious incision through the inflamed pleura revealed the lung immediately subjacent and adherent to the parietal pleura. An additional section of the posterior portion of the ninth rib was excised, revealing thick edematous pleura. Pus was then encountered at the lower medial margin of the operative field arising from under the tenth rib. Purulent exudate was found tracking beneath the tenth and eleventh ribs. The overlying portions of these two ribs were removed and a cavity was found which extended at least three to four inches below the eleventh rib. The cavity was about one inch in diameter and lined with purulent slough. From the walls of the cavity pus could be expressed. A tract was then discovered at the level of the tenth rib extending anteriorly. Digital examination of this tract revealed the smooth upper border of a rounded mass and some fleshy tissue was removed for examination from the depths of this anterior sinus. No further loculations were found and the entire cavity was packed. Culture of the pus was *Staphylococcus aureus*. Microscopic examination of the tissue removed (Dr. P. Klemperer) was as follows: Fragments of kidney showing leucocytic infiltration of the stroma with atrophy of the tubules and many leucocytes within the tubules; histology suggestive of pyelonephritis (see the history of an episode of right loin pain one year previous).

The postoperative course was one of progressive improvement. X-ray of the chest on the fifteenth postoperative day still showed some elevation and haziness of the diaphragm and slight thickening of the short fissure. Repeated urine examinations revealed only faint traces of albumin at times and occasional white cells. Culture of the urine was reported enterococcus. The patient was discharged with a clean granulating wound and normal temperature.

The interpretation of the pathogenesis in this case admits of several possibilities. The following statements appear warranted: the culture of the pus was staphylococci and the abscess was therefore presumably metastatic from the previous skin lesions; there was a spread of the infection through or behind the diaphragm; both the pleural and the perinephric spaces were invaded. In view of the acute onset with chills, fever, chest pain, and lung findings, in addition to the tardy appearance of loin pain, the supradiaphragmatic lesion was probably primary, and the perinephric space and kidney were secondarily invaded.

The lesion in the lung itself was probably a metastatic subpleural abscess with an area of consolidation about it. This type of lesion induces an early pleural reaction which tends to form adhesions between

onset. In our experience we have often found pneumococci of the higher types in the sputum of patients who have lung lesions subsequently proved not to be of pneumococcal origin, especially when the typing is done by the mouse method. By that method, even though there are only a few pneumococci present in the specimen of sputum injected into the peritoneal cavity of the mouse, the growth of those organisms is favored and that of the remaining is inhibited. Consequently that method gives no information as to whether or not the pneumococcus found was the predominant organism or merely one of a number of organisms present in the upper respiratory passages. As far as the prompt appearance of the physical signs of lobar consolidation is concerned, such findings are just as compatible with the picture of a staphylococcus abscess with surrounding pneumonitis as with pneumococcus lobar pneumonia. Finally, the extension of an independent renal and perirenal infection to the exact site of a pneumonic lesion with associated pleuritis would be too unusual a coincidence on which to reckon when a more likely pathogenesis can be offered.

SUMMARY

A case of staphylococcic empyema with extension beneath the diaphragm and about the kidney is presented. The anatomical pathways for spread of infection from the thorax to the subphrenic regions are discussed. Similar cases recorded in the literature are analyzed.

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region.¹⁰ This was the pathway postulated in the case reported by Tees,¹⁰ in which a lumbar abscess could be traced upward to an intrapulmonary empyema. The infection was directed away from the kidney by the sheath of the quadratus lumborum and the thick posterior layer of the renal (Gerota's) fascia. The efficacy of this fascial layer as a barrier against spread of infection toward the kidney was borne out by a case reported by Edelman.¹⁵ An exploratory operation was done for what was thought to be a perinephric abscess. Instead an abscess was found posterior to the posterior layer of the renal fascia, but immediately adjacent to it, and yet the fatty capsule of the kidney, separated only by this posterior layer of renal fascia, was entirely normal.

There is a pathway, however, which would carry a pleural infection anterior to the posterior layer of the renal fascia into direct contact with the kidney. Cunningham¹⁴ states that not infrequently "an interval separates the diaphragmatic fibers arising from the lateral lumbocostal arch from those arising from the medial lumbocostal arch. In these cases the kidney and the lower limit of the pleura are intimately related." In addition in this region the anterior and posterior layers of the renal fascia of Gerota fuse with the diaphragmatic fascia and do not present the distinct layers of thick protecting fascia that they do anteriorly, posteriorly, and laterally.¹² From the operative findings in the case which is the object of this report, it seems most probable that the infection reached the kidney through this defect between the diaphragmatic origins from the two lumbocostal arches.

In the final differential diagnosis of our case certain other possibilities must be mentioned. One interpretation that has the weight of statistical frequency to recommend it is the diagnosis of metastatic cortical abscess of the kidney with secondary perinephric abscess, perforation of the diaphragm, empyema, and pneumonitis. However, a careful analysis of the clinical history makes this diagnosis unsound. The onset of the illness was sudden with prompt appearance of symptoms and signs related to the lung. It was not until almost the sixth week of illness that severe back pain occurred, presumably the effect of spread beneath the diaphragm. Another feature is the fact that, with the exception of the skin and dental infections, the patient was well prior to the onset of this illness; whereas, in those cases of unsuspected subphrenic abscess that have as their first manifestation some supradiaphragmatic complication, there is usually a period of unexplained fever or vague chronic or subacute illness prior to the pulmonary or pleural infection.

There is also the possibility that two distinct illnesses were present, namely, a pneumococcus pneumonia and a staphylococcus renal cortical abscess, that spread upward to invade the pleura. The findings that support such a conclusion are presence of pneumococcus type XI in the sputum and the physical findings resembling lobar pneumonia at the

formed on at least four animals. The tampon material used was of different consistency. The very light hydrophilic spongy brocatamp was mainly used, as it appeared very effective in arresting hemorrhage from parenchymatous organs (liver). Tampon material soaked in a hemostatic agent (sangostop) was also used successfully. The material is exceedingly plastic and can be compressed into about one-twentieth of its volume. Tampons of greater consistency were employed to stuff large cavities.

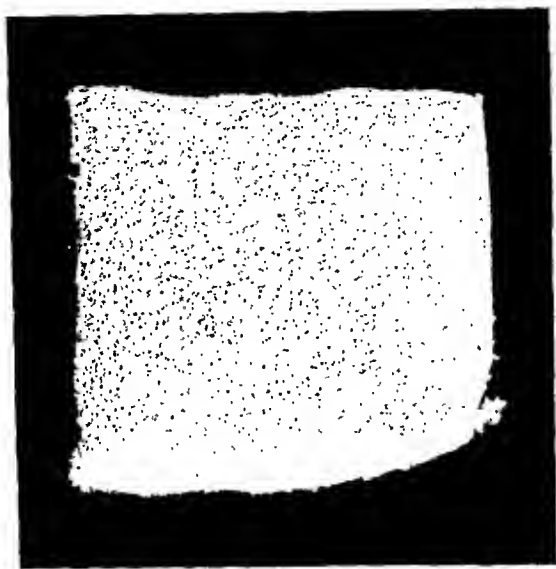


Fig. 1.—Photograph of spongeous tampon material.

There was no apparent difference in the reaction of soft or hard and compressed and noncompressed tampons. Apparently the spongy mass of the tampons soon becomes filled with serum which equalizes the differences. The reaction of the various tissues to the implanted tampons is a very slight one. There seems to be no chemical or mechanical irritation of the surrounding tissue. The collagen which forms the tampon does not act as a foreign body in the organism. The tampons do not become adherent to the surrounding tissue. During the first few days following the implantation, they apparently absorb serum. This is followed by an invasion of leucocytes which extend their phagocytic action along the large surface of the spongy tissue. The wide meshes and openings facilitate the infiltration of granulation tissue from the connective tissue capsule that soon develops around the tampon and is more or less firmly attached to the surrounding structures. Tampons in parenchymatous organs, such as the liver, spleen, kidneys, etc., are fixed; whereas, tampons in muscle, fat, and connective tissue remain loosely attached to their environment by a thin network of connective tissue fibers for considerable time.

EXPERIMENTS WITH TAMPONS AND MEMBRANES MADE OF COLLAGEN

H. FERIZ, M.D., LECTURER FOR SURGICAL PATHOLOGY, UNIVERSITY
OF AMSTERDAM, AMSTERDAM, HOLLAND

THE use of animal absorbable and assimilable material in surgery has been confined practically to catgut. The use of devitalized connective tissue, recommended by Nageotte,¹ on good theoretical and experimental bases has never become popular. The present development of resistant fiber from dissolved collagen creates the possibility for experimental investigations on absorbable tampons.

The surgical importance of an absorbable or assimilable tampon material is evident. It would no longer be necessary to leave a foreign body in the body disturbing and delaying the healing of the wound by the presence and ultimate removal of an unabsorbable tampon. All the dangers associated with the removal of a tampon, such as injury to the adhering organs, reopening of cavities, spreading of localized infections by rupture of granulation tissue, secondary hemorrhage by tearing away clots of blood, etc., would be obviated and patients would be spared the pain associated with manipulation of tampons. Moreover, the field of application of an absorbable biologic, nonirritating material could be widely extended as compared with that of the tampon now in use. The material, originally intended to be the substance of a new absorbable suture, is obtained from slaughtered cattle. In addition to ligatures and sutures tampons and *plombes* can be made of the same collagen material.

Before testing these tampons surgically, in which we are still engaged, it was necessary to examine the reaction of the organism to the implantation of these collagen fibers and to determine whether the implanted material would behave in the body as a foreign body, or whether it would be absorbed, assimilated, or organized. It was taken for granted that the reaction of the body to the new material would be different from that to catgut. Apart from the devitalization and denaturalization process the material has undergone, the substances of the two materials are quite different, for catgut is made of the smooth muscle tissue of sheep's intestine. In histologic sections using van Gieson's stain, catgut appears yellowish brown. The new material, brocatamp, on the contrary, consists of connective tissue substance, and the collagen reaction reveals a slightly red color to van Gieson's stain. Our first experiments were made exclusively for the purpose of studying the histologic changes of the material in animal tissue and the reaction of this tissue to the implanted material. Each experiment was per-

in gaps of this material similar to osteoclasts in the region of a fracture. The number and the activity of the leucocytes vary largely. Probably secondary factors, namely, tissue injury and necrosis of the surrounding tissue by the operation or by infection, play an important part. The collagen per se of the tampon material has no leucotropic action. Therefore, the tampon, as a rule, does not suppurate, unless infected cavities are tamponed or an abundant use is made of tincture of iodine in the wound. Then the process of organization is confined to the envelopment of the tampon that is totally destroyed by leucocytes. However, even these focal infections disturb the histologic appearance of the surrounding tissue astonishingly little. The resorption period of the tampon, i.e., the time in which the implanted material either dissolves or is made part of the organism by organization, depends on the size of the tampon, the vascularity of the surrounding area, and the quality of the tampon material. Generally large tampons remain longer than small ones and vascular tissues, such as the spleen or the liver, enhance absorption. The structure of the tampon surface is also important. The more porous the material, the more rapid is the process of organization. For these reasons it is not possible to determine definitely the time required for absorption. In some instances the fibers of the tampon material cannot be recognized six weeks after implantation; whereas, in others distinct rests of the spongy material may be observed even after six months.

In more than 100 experiments there was not a single case in which the tampon was extruded, even from an infected area. On the contrary, it seems that the presence of pus promotes the digestion of the tampon material. Instead of the tampon, there was found an encapsulated caseous area which, on microscopic examination, did not show any tampon fibers. It consisted solely of fatty leucocytes. When the reaction of the organism is neither disturbed nor interrupted, after a varying period of time there remains a connective tissue cicatrix that is much smaller than the original tampon. When a large tampon has been used, this end effect will be reached only after a year. Smaller tampons are organized much more quickly.

The minimal degree of irritation to the surrounding tissue is impressive. The simultaneous occurrence of the processes of organization and destruction of the implanted material is quite characteristic. This is demonstrated clearly in Figs. 1 to 8 (Rabbit 99) which were made by L. H. Bretschneider, histologist of the Zoological Laboratory of the State University at Utrecht. On June 1, 1938, a large tampon was placed into the subcutaneous fat through an incision in the skin of the abdominal wall of an experimental animal. The cavity had been treated previously with tincture of iodine. On Jan. 18, 1939, the tampon, together with the surrounding abdominal wall, was extirpated. The tampon could be palpated as a firmly elastic, subcutaneous mov-

The connective tissue capsule of the implanted body is formed by organization of the serum in and around the tampon. Under normal conditions the tampon is not as firmly encapsulated as a foreign body, but rather is infiltrated by granulation tissue and thus gradually organized. Accompanying this process of organization is one of destruction not only by phagocytosis but also by liquefaction. The leucocytes and giant cells particularly show a phagocytic activity. The latter appear as syncytial formations of connective tissuelike origin. They are often seen pressed close to the fibers of the implanted material or

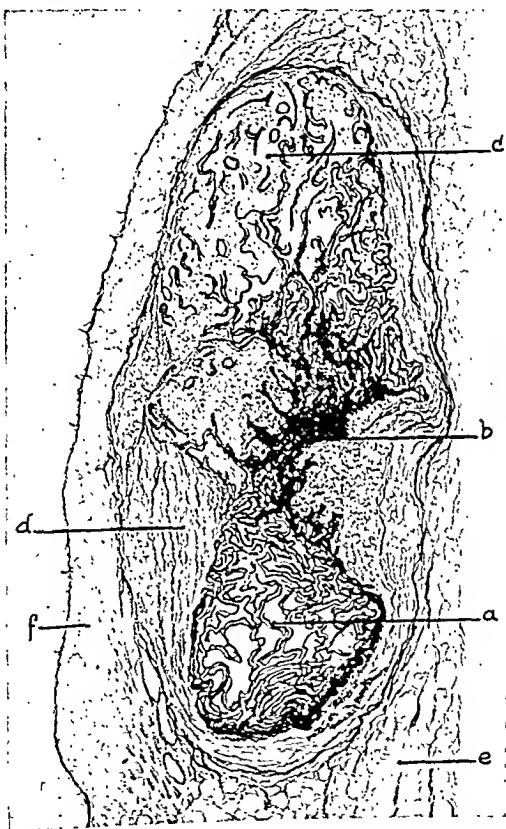


Fig. 2.—Appearance on microscopic examination of implanted tampon. The entire tampon rest is surrounded by a fibrillar connective tissue capsule which is very thick in some places and remarkably thin in others. These connective tissue fibers lie also between skin and implanted material. The skin is not fixed to the tampon. The latter shows different structures and colors. In some places it is hardly impaired and only infiltrated by serous fluid (a). In other places the typical fibrous structure of the material has disappeared (b); here are found caseous and crumbling masses in the midst of which are foci of leucocytes that are mostly necrotic (pyknosis, caryorrhexis, caryolysis, fattening, etc.). In many places the rests of the material, stained with eosin-hematein and varying in general from a light to a dark red color, are violet blue; especially the periphery of the fibers shows this discoloration as well as a somewhat crystalline structure which, according to the silver nitrate reaction, appeared to be chalk. Apart from the destruction of the tampon material at the site of the masses of leucocytes described above, there is observed in the greater part of the periphery of the tampon (c) an advanced fibrous organization and substitution of the implanted material. Here the fibers of the tampon material are broken up, ruptured, and surrounded by fresh connective tissue which gradually merges with the fibrils of the capsule. This process of organization is completed in some areas (d); e represents subcutaneous tissue, and f skin.

in gaps of this material similar to osteoclasts in the region of a fracture. The number and the activity of the leucocytes vary largely. Probably secondary factors, namely, tissue injury and necrosis of the surrounding tissue by the operation or by infection, play an important part. The collagen per se of the tampon material has no leucotropic action. Therefore, the tampon, as a rule, does not suppurate, unless infected cavities are tamponed or an abundant use is made of tincture of iodine in the wound. Then the process of organization is confined to the envelopment of the tampon that is totally destroyed by leucocytes. However, even these focal infections disturb the histologic appearance of the surrounding tissue astonishingly little. The resorption period of the tampon, i.e., the time in which the implanted material either dissolves or is made part of the organism by organization, depends on the size of the tampon, the vascularity of the surrounding area, and the quality of the tampon material. Generally large tampons remain longer than small ones and vascular tissues, such as the spleen or the liver, enhance absorption. The structure of the tampon surface is also important. The more porous the material, the more rapid is the process of organization. For these reasons it is not possible to determine definitely the time required for absorption. In some instances the fibers of the tampon material cannot be recognized six weeks after implantation; whereas, in others distinct rests of the spongy material may be observed even after six months.

In more than 100 experiments there was not a single case in which the tampon was extruded, even from an infected area. On the contrary, it seems that the presence of pus promotes the digestion of the tampon material. Instead of the tampon, there was found an encapsulated caseous area which, on microscopic examination, did not show any tampon fibers. It consisted solely of fatty leucocytes. When the reaction of the organism is neither disturbed nor interrupted, after a varying period of time there remains a connective tissue cicatrix that is much smaller than the original tampon. When a large tampon has been used, this end effect will be reached only after a year. Smaller tampons are organized much more quickly.

The minimal degree of irritation to the surrounding tissue is impressive. The simultaneous occurrence of the processes of organization and destruction of the implanted material is quite characteristic. This is demonstrated clearly in Figs. 1 to 8 (Rabbit 99) which were made by L. H. Bretschneider, histologist of the Zoological Laboratory of the State University at Utrecht. On June 1, 1938, a large tampon was placed into the subcutaneous fat through an incision in the skin of the abdominal wall of an experimental animal. The cavity had been treated previously with tincture of iodine. On Jan. 18, 1939, the tampon, together with the surrounding abdominal wall, was extirpated. The tampon could be palpated as a firmly elastic, subcutaneous mov-

The connective tissue capsule of the implanted body is formed by organization of the serum in and around the tampon. Under normal conditions the tampon is not as firmly encapsulated as a foreign body, but rather is infiltrated by granulation tissue and thus gradually organized. Accompanying this process of organization is one of destruction not only by phagocytosis but also by liquefaction. The leucocytes and giant cells particularly show a phagocytic activity. The latter appear as syncytial formations of connective tissuelike origin. They are often seen pressed close to the fibers of the implanted material or

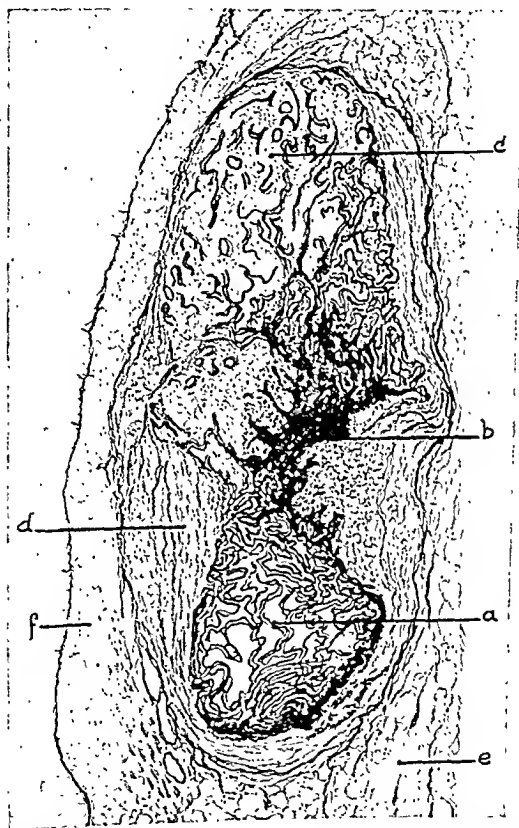


Fig. 2.—Appearance on microscopic examination of implanted tampon. The entire tampon rest is surrounded by a fibrillar connective tissue capsule which is very thick in some places and remarkably thin in others. These connective tissue fibers lie also between skin and implanted material. The skin is not fixed to the tampon. The latter shows different structures and colors. In some places it is hardly impaired and only infiltrated by serous fluid (*a*). In other places the typical fibrous structure of the material has disappeared (*b*); here are found caseous and crumbling masses in the midst of which are foci of leucocytes that are mostly necrotic (pyknosis, karyorrhexis, karyolysis, fattening, etc.). In many places the rests of the material, stained with eosin-hematein and varying in general from a light to a dark red color, are violet blue; especially the periphery of the fibers shows this discoloration as well as a somewhat crystalline structure which, according to the silver nitrate reaction, appeared to be chalk. Apart from the destruction of the tampon material at the site of the masses of leucocytes described above, there is observed in the greater part of the periphery of the tampon (*c*) an advanced fibrous organization and substitution of the implanted material. Here the fibers of the tampon material are broken up, ruptured, and surrounded by fresh connective tissue which gradually merges with the fibrils of the capsule. This process of organization is completed in some areas (*d*); *e* represents subcutaneous tissue, and *f* skin.

tincture of iodine and there was the danger of secondary infection from the skin wound. However, in spite of this, the tampon was not extruded. It appeared that even the skin had not become adherent to the implanted body. In other tissues and in parenchymatous organs in which the reactions produced by the tampon are less liable to the disturbing action of exogenous factors (operative trauma, infection, wound healing), the processes of absorption and organization of

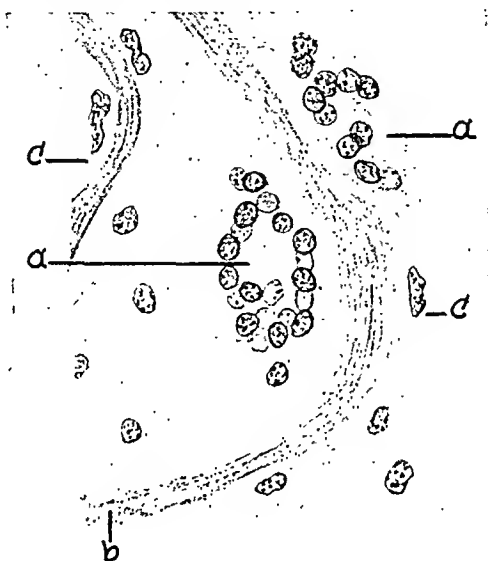


Fig. 5.—Drawing of microscopic appearance of histologic section of tampon material showing: *a*, phagocytic giant cells on tampon fibers; *b*, autolysis of tampon fibers by ferment action resulting in granular and frayed appearance of the fibers; *c*, fibroblasts. (Enlarged oil-immersion Bausch and Lomb, 1.25, ocular 10.)

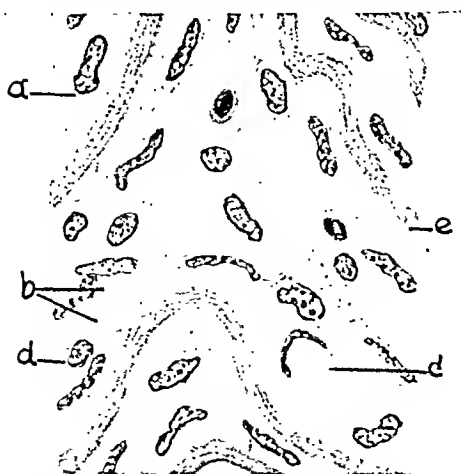


Fig. 6.—Histologic section of implanted tampon material showing beginning organization of the intertubular exudate: *a*, young fibroblasts; *b*, fibroblasts with collagen fibers; *c*, young capillary vessels; *d*, fat cells; *e*, partly granulated tampon fibers (beginning of destruction). (Enlarged oil-immersion Bausch and Lomb, 1.25, ocular 5.)

able nodule of about one-half inch in diameter. It was placed in formalin, sectioned, and stained with hematoxylin-eosin. On microscopic examination the implanted material appeared encapsulated between the fascia and the subcutaneous tissue showing focal necrosis in the center with leucocytic infiltration, giving it the appearance of ground glass. In some parts the tampon was considerably absorbed; whereas, other areas revealed various stages of absorption and substitution by granulation tissue and connective tissue. A few rests of the tampon at the periphery mark the border of the implanted body.

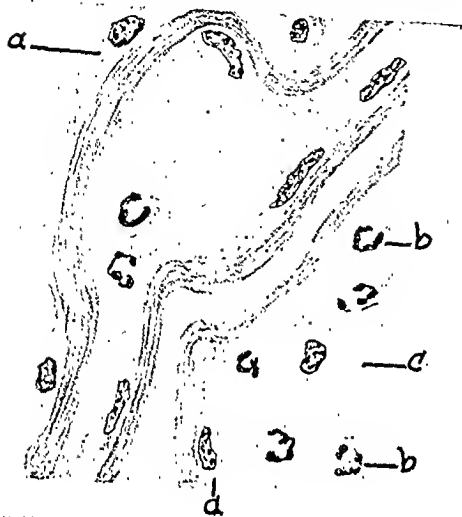


Fig. 3.



Fig. 4.

Fig. 3.—Drawing of microscopic section of tampon material showing serous exudation and infiltration of leucocytes and fibroblasts. The fibroblasts lie adjacent to the tampon material and the leucocytes in the serous exudate. *a*, Fibroblasts; *b*, leucocytes; *c*, serous exudate. (Enlarged oil-immersion Bausch and Lomb, 1.25. ocular 5.)

Fig. 4.—Drawing of microscopic appearance of section of tampon material, showing invasion of young connective tissue cells between unimpaired tampon fibers. (Enlarged oil-immersion Bausch and Lomb, 1.25. ocular 5.)

Thus, two absolutely different types of the absorption process are observed: (1) fibroblastic infiltration associated with invasion of giant cells whose absorption function is most apparent where they affect the tampon material (corrosion of the tampon fibers) (Figs. 5 and 6); (2) leucocytic infiltration with focal necrosis and destruction of the tampon material (Figs. 3 and 8).

In both cases the tampon is gradually replaced by granulation tissue (Figs. 5, 6, and 8). Gradually the oval connective tissue cells with collagen fibers and vascular endothelium become predominant. Young collagen connective tissue appears and the original boundary between the organized implanted body and the capsule is no longer perceptible.

It is a well-known fact that the subcutaneous fat tissue of the abdominal wall is poorly suited for absorption of an implanted body. Moreover, in this particular experiment the tissue was irritated by

tincture of iodine and there was the danger of secondary infection from the skin wound. However, in spite of this, the tampon was not extruded. It appeared that even the skin had not become adherent to the implanted body. In other tissues and in parenchymatous organs in which the reactions produced by the tampon are less liable to the disturbing action of exogenous factors (operative trauma, infection, wound healing), the processes of absorption and organization of

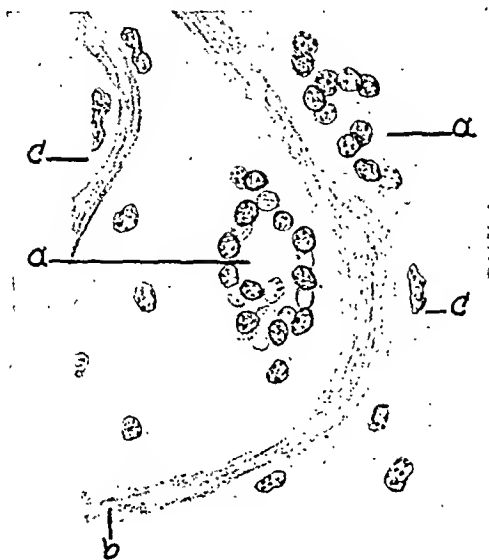


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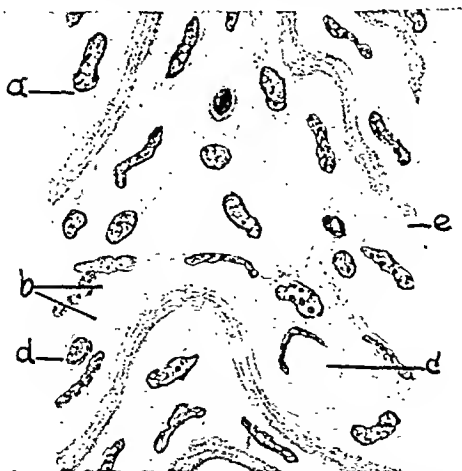


Fig. 6.—Histologic section of implanted tampon material showing beginning organization of the interfibrillar exudate: *a*, young fibroblasts; *b*, fibroblasts with collagen fibers; *c*, young capillary vessels; *d*, fat cells; *e*, partly granulated tampon fibers (beginning of destruction). (Enlarged oil-immersion Bausch and Lomb, 1.25, ocular 5.)

the incorporated material occur less equally. But in these cases, also, these two processes, namely the destruction of the implanted material and the secondary organization by granulation tissue and by primary connective tissue growth, as a result of fibroblastic invasion of the unimpaired fibers of the implanted body are almost always recognizable. This primary growth of connective tissue, in my opinion, is due to the affinity between the fibroblasts and the collagen substance that evidently can be used immediately by the young cells for the construction of new fibers. Apparently the same forces are operative in this case as in the rehabilitation of Nageotte's *greffes mortes*. Indeed, in some very compact parts of the implanted bodies that resist the penetration of serum longest, some adult oval cells are found quite isolated

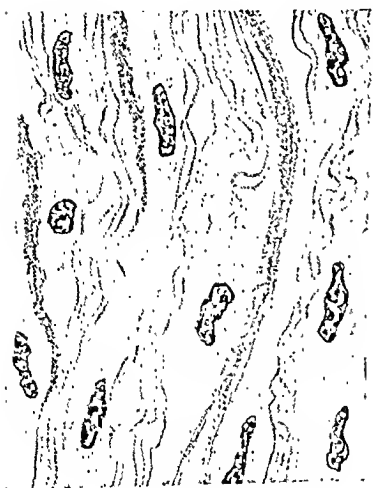


Fig. 7.



Fig. 8.

Fig. 7.—Histologic section of implanted tampon material, showing advanced connective tissue-like organization and destruction of the tampon fibers which lose their fibrous structure. (Enlarged oil-immersion Bausch and Lomb, 1.25. ocular 10.)

Fig. 8.—Histologic section of implanted tampon material at borders of the destructive center, shown by *b* in Fig. 3. *a*, Granular mass of tampon material (stained dark red in the preparation) with focal areas of leucocytes; *b*, necrobiotic leucocytes; *c*, beginning destruction and fragmentation of tampon fibers; *d*, unimpaired tampon fibers. (Enlarged oil-immersion Bausch and Lomb, 1.25. ocular 5.)

from the living tissue at the periphery, and in such close contact with the collagen fibers of the implanted body that it is clearly a question of a genuine rehabilitation. The structure of the tampon here appears to be readily habitable for connective tissue cells. As a rule this primary fibrous organization prevails in the deeply implanted and compact tampons that are least exposed to disturbances (Fig. 3) and that resist best the serocellular infiltration and consequent ferment and phagocytic actions of the leucocytes. In noncompressed tampons and in those lying in operative wounds the destructive processes be-

come more prominent and, in an infected tissue, may even culminate in the destruction of the material by pus and the encapsulation of the necrosis as described above.

CONCLUSIONS

The characteristics of a new, assimilable material that might be useful in surgery, namely, for tamponade and isolation of tissues and organs, were studied experimentally and the result described. The material, brocatamp,* consists of collagen and appears perfectly non-irritating to the surrounding tissues when implanted in rabbits.

It is partly absorbed by the lytic activity of ferments and by phagocytosis, and partly organized either by direct infiltration of connective tissue cells or by the formation of granulation tissue.

REFERENCE

1. Nageotte: L'organisation de la matière (les greffes mortes), Paris, 1922, p. 83.

*Brocatamp was kindly placed at my disposal by Messrs. N. V. Koninklijke Pharmaceutische Fabrieken v.h. Brocades-Stheeman and Pharmacia Meppel.

SOLITARY TRUE DIVERTICULUM OF THE CECUM

REPORT OF A CASE

JAMES C. OWINGS, M.D., AND ZACHARIAH MORGAN, M.D., BALTIMORE, MD.

SOLITARY true diverticula of the cecum seem to be quite rare, since in a recent article Bennett-Jones¹ was able to collect only nineteen cases and added three, the treatment of which he had observed. However, he makes the statement, which is very likely true, that probably there have been a good many other cases that have not been reported because of poor or fatal results or else that they have been reported in obscure journals. We wish to add one more case to those already reported.

Mrs. E. P., white woman, aged 42 years, had been under treatment by one of us (Dr. Z. Morgan) since September, 1933, for a mild thyroid and pituitary deficiency. During this period she had had occasional attacks of abdominal pain localized to the right lower quadrant which were suggestive of recurrent appendicitis. Her past and family histories were relatively unimportant, except that she had developed an incisional hernia following a cesarean section in 1935. This hernia was becoming larger and commencing to give her trouble. She had had typhoid fever at 18 years of age, a tonsillectomy and an appendectomy in 1925, and a benign tumor removed from the right breast in 1934.

She was admitted to the Church Home Hospital on April 7, 1939, after having suffered with severe abdominal pain for the previous four days. The pain, which at first seemed to be generalized over the whole abdomen, had been associated with nausea and fullness. By the time she was admitted, the symptoms had become localized to the right side. She had not vomited, and bowel movements had been normal.

Examination on admission showed her temperature to be 98.6° F., pulse 84, respirations 20, blood pressure 140/80, hemoglobin 72 per cent and white blood count 12,250. She was in no particular pain at the time of examination, complaining only of soreness in the right side. Examination of the abdomen revealed marked tenderness with reflex muscle spasm at McBurney's point. There was an old mid-line scar with a fairly marked hernial defect at its upper angle. Otherwise the examination was essentially negative. A diagnosis of subsiding appendicitis and incisional hernia was made. Operation was advised, and the patient consented.

The abdomen was explored through the old incision, with the idea of repairing the hernia at the same time the appendix was removed. Gas-ether anesthesia was used. Upon opening the peritoneum, a large hard mass with a crater in its center was felt in the lateral wall of the cecum directly opposite the ileocecal valve, and there were some hard glands present in the mesentery. There was no evidence of any obstruction. The cecum was exposed, and even under direct vision it was impossible to tell whether we were dealing with an inflammatory process or a new growth. In view of this uncertainty, it was thought best to do a wide resection, so the right side of the colon, including the cecum and terminal ileum, was removed in a single block. The end end of the transverse colon was inverted, and an aseptic

end-to-side anastomosis was performed between the ileum and transverse colon with Stone's clamps. The hernia at the upper angle of the incision was repaired in the usual manner. The patient had a very uneventful postoperative course.

The pathologic report on the specimen (Dr. V. H. Norwood) was: "Diverticulum of the cecum (true), showing acute inflammation with ulceration and a large fecalith. Appendicitis acute secondary."

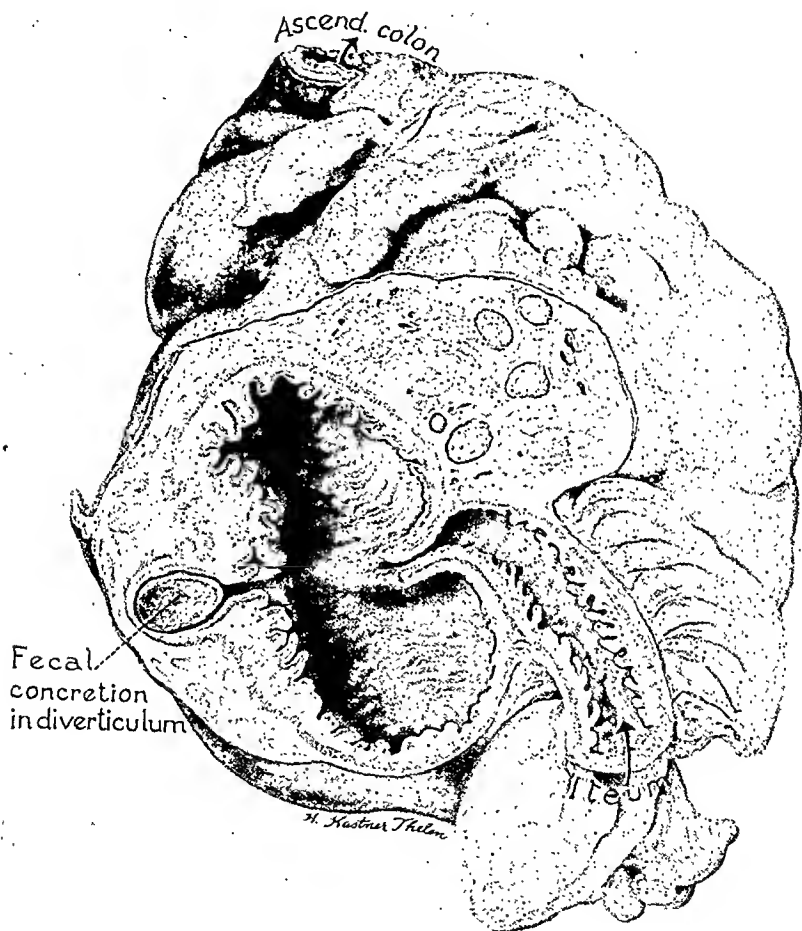


Fig. 1.

On April 20, thirteen days following the original operation, the patient, while bathing, noticed a small lump in the right breast, which she called to our attention. Upon examination the lump was found to be about the size of a small hazelnut. It was freely movable, being deeply buried in a rather large fatty breast and apparently not attached either to the skin or underlying tissue. Since the patient was very fearful of carcinoma of the breast, she was advised to have the lump removed more for her mental satisfaction than any other reason. The nodule was removed under local anesthesia on April 25, and, much to our surprise, the routine frozen section showed medullary carcinoma. The next day a simple mastectomy was done, with the removal of the lower axillary glands and the fascia over the pectoral

muscles. A radical operation was not done because of the very small size of the growth. Again she had a quite uneventful postoperative course and was discharged from the hospital on May 7. Following discharge she was given a full course of radiation. She has had no evidence of recurrence to date and no symptoms referable to the partial resection of the colon. On July 7 she was carefully fluoroscoped, and x-rays of a barium enema were made in an attempt to discover diverticula elsewhere in the colon. The report of this examination is as follows (Dr. Piersou): "Cecum and ascending colon have been resected. The anastomosis is working perfectly. No diverticula demonstrated."

This case follows very closely the pattern shown by previously reported cases, in that the usual preoperative diagnosis was acute appendicitis and that, when a large mass was found on the wall of the cecum, it was impossible to tell whether it was malignant or not, so a wide resection was done to play safe. The end result was also in accord, since to date only one death has been recorded in this type of case. In a good many cases there was only a very small diverticulum which was treated by local excision and closure of the neck. There were nine cases in which the mass was large enough to make the diagnosis doubtful and which, therefore, required resection. The one death occurred in this group. Obviously, local excision is the procedure of choice if the size of the lesion permits. The only unusual feature about our case was that the patient, while bathing during the postoperative course from her first operation, accidentally discovered a small nodule in her breast. This nodule was a carcinoma and required removal of the breast.

REFERENCE

1. Bennett-Jones, M. J.: Primary Solitary Diverticulitis of the Cecum, a Report of Three Cases With a Review of Seventeen Recorded Cases, *Brit. J. Surg.* 25: 66, 1938.

CONGENITAL HOURGLASS BLADDER

NELSE F. OCKERBLAD, M.D., AND HJALMAR E. CARLSON, M.D.,
KANSAS CITY, MO.

THE condition known as congenital hourglass bladder can be considered one of the rarer anomalies, with a total of sixteen cases now in the literature. It may be defined as a congenital anomaly in which the bladder is divided into two smaller cavities by a transverse constriction, without definite change in total volume and without change in the component parts of the bladder wall except at the constriction where the bladder is twice the normal thickness. The constriction may occur either above or below the ureteral orifices. Congenital hour-glass bladder must be distinguished from hourglass deformities of the bladder due to other causes such as (1) diverticulum, (2) patent urachus, (3) vesica duplex or vesica bipartita, (4) absence of the prostate and seminal vesicles, either congenital or surgical, and (5) constriction due to inflammatory conditions such as tuberculosis or severe cystitis, or as a result of extrinsic or intrinsic injury.

ETIOLOGY

The condition of congenital hourglass bladder must have some reasonable embryologic basis for its occurrence, and various theories have been proposed. These theories have been well summarized by Eisenstaedt and McDougall,¹ who have divided them into three groups as follows:

1. Atavistic relationship or hourglass bladder normally found in some animals.
2. Persistence of the embryonic ureteric membrane.
3. Unequal growth of the two bladder anlagen.

The atavistic relationship to the hourglass bladder found in lower animals was suggested by Krasa and Paschke² who found many types of hourglass bladder in a variety of animals. The persistence of the embryonic membrane of the ureter as the etiological factor was suggested by Chwalla³ as a result of studies of Hoehstetter's embryos in which he found such a membrane in a 37 mm. embryo. Ordinarily this membrane disappears before the 28 mm. stage. The theory of unequal growth of bladder anlagen was first stated by Pagenstecher,⁴ and later by Gruber⁵ who believed that there is a failure of perfect union of the trigonal portion which is of mesodermal origin and the bladder proper which is of endodermal origin. In regard to the latter theory, we must remember that it is only the lining of the bladder which is endodermal. The bladder musculature is mesoderm and is, therefore, of the same material as the trigone. At the present time we believe that the evidence for or against either of these theories is insufficient upon which to draw a reasonable conclusion.

muscles. A radical operation was not done because of the very small size of the growth. Again she had a quite uneventful postoperative course and was discharged from the hospital on May 7. Following discharge she was given a full course of radiation. She has had no evidence of recurrence to date and no symptoms referable to the partial resection of the colon. On July 7 she was carefully fluoroscoped, and x-rays of a barium enema were made in an attempt to discover diverticula elsewhere in the colon. The report of this examination is as follows (Dr. Pierson): "Cecum and ascending colon have been resected. The anastomosis is working perfectly. No diverticula demonstrated."

This case follows very closely the pattern shown by previously reported cases, in that the usual preoperative diagnosis was acute appendicitis and that, when a large mass was found on the wall of the cecum, it was impossible to tell whether it was malignant or not, so a wide resection was done to play safe. The end result was also in accord, since to date only one death has been recorded in this type of case. In a good many cases there was only a very small diverticulum which was treated by local excision and closure of the neck. There were nine cases in which the mass was large enough to make the diagnosis doubtful and which, therefore, required resection. The one death occurred in this group. Obviously, local excision is the procedure of choice if the size of the lesion permits. The only unusual feature about our case was that the patient, while bathing during the postoperative course from her first operation, accidentally discovered a small nodule in her breast. This nodule was a carcinoma and required removal of the breast.

REFERENCE

1. Bennett-Jones, M. J.: Primary Solitary Diverticulitis of the Caecum, a Report of Three Cases With a Review of Seventeen Recorded Cases, *Brit. J. Surg.* 25: 66, 1938.

OCKERBLAD AND CARLSON.

| | | | | | | | | | No data by author |
|--|----|---|-------|--|-----------------|--|---|---|-------------------|
| Pieleke, O., 1904 ¹³ | 75 | M | Lower | Upper cavity twice size of lower | Size of quarter | Difficulty all his life. Nocturia and hematuria for 10 years; stoppage for 10 years. Used catheter | Cystotomy; diverticulum; drained by Witzel tube | Recovered from operation. Died 1 year later from uremia | |
| Fischer, H., 1910 ¹⁴ | | | | | | | | | |
| Caulk, J. R., 1920 ¹⁵ | 42 | M | Lower | Upper larger than lower | Not stated | Enuresis until 9 years of age. Dysuria for 9 years. Acute retention. | Suprapubic cystotomy, with resection of base of bladder | Recovered | |
| Caulk, J. R., 1920 ¹⁵ | 42 | F | Lower | Bladder contracted. Capacity 150 c.c. | Not stated | Intermittent dysuria for 11 years | Suprapubic cystotomy, with resection of base of bladder | Reflux up right ureter. Recovered | |
| Kretschmer, H. L., 1923 ⁸ | 83 | M | Lower | Lower cavity slightly larger than upper cavity | Not stated | Dysuria for 12 years | Suprapubic cystotomy | Died 8 days postoperative. Autopsy | |
| Kearns, W. M., and Taub, S. M., 1933 ¹⁶ | 22 | F | Lower | Lower segment larger than upper (by cystogram) | 2 cm. | Difficulty since early childhood. Hematuria | Upper cavity resected. Tightening of ureteral orifice. Nephrectomy | Hydronephrosis due to reflux. Recovered | |
| Eisenstadt, J. S., and McDougall, T. G., 1936 ¹ | 42 | M | Lower | Equal in size (by cystogram) | Three fingers | Enuresis until 14 years of age. Dysuria since | Entire muscle band excised | Diverticulum from upper cavity. Recovered | |
| Ockerblad, N. F., and Carlson, H. E., 1940 | 63 | M | Lower | Equal in size | 2 cm. | Nocturia 5 to 6 years; difficulty 3 years; with increasing incontinence and hematuria. Self catheterization for 6 months | 1. Suprapubic cystotomy and excision of muscle band 2. Transurethral resection of prostate | Recovered. Well five years later | |

TABLE I

| AUTHOR AND YEAR | AGE | SEX | LOCATION OF URETERS | RELATIVE SIZE OF CAVITIES | SIZE OF OPENING | SYMPTOMS | TREATMENT | REMARKS |
|-------------------------------------|-----|-----|---------------------|---|--------------------------------|---|---|---|
| Pusso, 1848 ⁶ | | | Lower | | | | | |
| Cutler, 1854 ⁰ | 11 | M | Not stated | Not stated | Small | Dysuria for one year. Blood and pus in urine | Expectant | Spontaneous rupture of abscess in right inguinal region. Death from bilateral pyonephrosis |
| Fothergill, 1878 ¹⁰ | | | Lower | | | | | |
| Detweiler, E. L., 1888 ⁷ | 69 | M | Upper | Compartments about equal. Diverticulum of upper cavity size of walnut, which abscessed into groin | Admitted point of index finger | Dysuria 3 to 4 years, with incontinence. Dyspepsia and debility | Incision and drainage of abscess in groin and scrotum. Urethral dilatation | Urethral stricture. Death. Autopsy showed left pyonephrosis and pyoureter |
| Muller, 1895 ¹¹ | | F | Lower | | | | | |
| Fuller, E., 1900 ¹² | 55 | M | Upper | Not stated | Two fingers; oval | Gradual increasing difficulty since childhood, hematuria 2 to 3 weeks | 1. Perineal section 2. Suprapubic cystotomy with incision of band with scissors. | Urethral stricture (postgonorrheal). Patient recovered. |
| Fuller, E., 1903 ¹² | 44 | M | Upper | Capacity lower cavity 1 to 1½ oz. Upper cavity twice size of lower cavity. Both lined with transitional stratified epithelium | Barely one finger; circular | Gradual increasing difficulty since childhood | 1. Perineal section 2. Suprapubic cystotomy with incision of band with scissors. | Urethral stricture (postgonorrheal). Small stone. Died 10 days postoperative from uremia. Autopsy |
| Pfecke, O., 1903 ¹³ | 34 | M | Lower | Upper cavity size of an apple. Size of lower cavity not stated | Three marks coin; oval | Obstipation with intermittent diarrhea. Palpable tumor. No urinary symptoms | Not stated | Bladder projected above symphysis |

identification of these two conditions. The differentiation of a congenital hourglass bladder from a congenital absence or surgical absence of the prostate and seminal vesicles should not be difficult. An hourglass constriction of the bladder due to inflammation, such as chronic cystitis or tuberculosis, or to either extrinsic or intrinsic injury is conceivable, but that it would ever approach a condition closely resembling that of a congenital hourglass bladder is extremely unlikely. Certainly, however, an hourglass type of bladder with a large communication may be regarded with suspicion.

TREATMENT

The treatment of congenital hourglass bladder should be directed toward enlargement of the opening between the two halves of the hourglass so as to allow better drainage and more complete emptying of the bladder. Since the total capacity in these cases closely approaches that of the normal bladder, it seems more plausible to follow some procedure concerned with the eradication of the fibrous ring rather than to remove the upper portion of the hourglass as would generally be done with a diverticulum. Where the ureters empty into the upper half, there is, of course, no choice in the matter. Of the sixteen patients, nine were operated upon. Two had suprapubic cystotomy only. In six, some type of operation directed at removal of the fibrous ring was done, and in one in whom the upper cavity was small, a resection was done. Of the six cases in which the fibrous ring was removed, the base of the bladder was resected in two; in two cases the ring was cut with a scissors; and in two the entire muscle band was excised. Of the nine patients who underwent operation, six recovered and three died.

CASE REPORT

W. H. M., No. L-50673, white male, a physician, aged 63 years, was admitted to the hospital on April 14, 1934. He complained that for the past five or six years he had had an increasing nocturnal frequency and that for the past three years he had had increasing difficulty of urination, with a developing urgency and increasing incontinence with some hematuria. For the past six months he had been catheterizing himself daily, with the exception of the past month when he used the catheter every eight hours.

Examination showed the presence of an ankylosing osteoarthritis of the spine, sacroiliac joints, and one hip joint. Rectal examination suggested an enlarged prostate.

Laboratory examination showed the urine to be alkaline, with a specific gravity of 1.013, albumin 4 plus, no sugar, and with 20,200 pus cells per cubic millimeter and 3,200 red blood cells per cubic millimeter on microscopic examination. The blood showed a red blood cell count of 3,920,000, a white blood cell count of 9,000, and hemoglobin, 78 per cent. The Wassermann and Kahn tests were negative. The intravenous phenolsulphonphthalein test showed a total output of 27 per cent in one hour.

Cystoscopic examination showed a small median bar with a bladder of evidently greatly diminished size. The bladder was full of debris, and the mucosa showed the presence of a rather severe chronic cystitis. There was an opening about 2 cm. in diameter in what appeared to be the dome of the bladder. An air cystogram was then taken which revealed the presence of an hourglass deformity (Fig. 1).

INCIDENCE

It is a little difficult to separate in the literature the congenital hourglass bladder from the hourglass deformities of other etiology, since a certain degree of confusion exists. However, we have succeeded in collecting sixteen such cases, including a case of our own, which are summarized in Table I.

The first description fulfilling the requirements of a congenital hourglass bladder was by Passo in 1848. An exact description of the autopsy findings is given which leaves no doubt as to the condition found.⁶ The first use of the term hourglass bladder in relation to the congenital type was by Detwiler in 1888.⁷ It is probable, however, that the name had previously been used in describing bladders with diverticula.

The condition to date has been more frequent in men than in women. Of the sixteen cases, ten were in males and three in females, and in three the sex was not stated. The age was extremely variable. The youngest patient was 11 years old, as described by Cutter,⁸ and the oldest was 83, as described by Kretschmer and Morris.⁹ The average age of twelve cases was 48.5 years.

DIAGNOSIS

The symptoms of congenital hourglass bladder were quite variable, but, as might be expected, 66 per cent of all persons complained of life-long bladder disturbance. The early symptoms include urinary difficulty, dysuria, or a history of enuresis. The symptoms of urinary difficulty and dysuria continue into later life and eventually bring the patient to the doctor. Thirty-three per cent, however, had no symptoms until later in life. Two patients had acute urinary retention, and one had hematuria. It has been suggested that it is the superimposing of a cystitis on the congenital deformity that produces most of the disturbance. The patient presented by us had a severe cystitis with an extremely purulent urine.

On cystoscopic examination, the bladder is found to be divided into two cavities, one above the other, which are connected by an opening from one to three fingers in width. The ureters may open either into the lower or the upper compartment. The relative size of the two compartments is variable, but the combined capacity of the two compartments is that of a normal bladder. The margin of the opening is seen to be thick, is generally twice the thickness of the bladder wall, and does not present the shelflike edge seen in the opening to a diverticulum. When the cystoscope is introduced into the upper cavity, normal trabeculations and normal vessel markings are seen. We, therefore, have two distinct cystoscopic features to differentiate congenital hourglass bladder from an hourglass deformity due to a diverticulum. Congenital hourglass bladder can be differentiated from hourglass deformity due to a persistent urachus since the contours of the hourglass bladder are rounded and it does not have the spiked upward extension seen with a patent urachus. If there is any doubt, a cystogram will assist in the

3. The condition is most common in males, in a ratio of ten to three. The youngest patient was 11 years of age, and the oldest 83 years of age, with an average age of 48.5 years.

4. Sixty-six per cent of the patients evidently had had some urinary disturbance since early life, including urinary difficulty, dysuria, or enuresis. Thirty-three per cent had no symptoms until later in life. It is probable that the development of a severe cystitis in a patient with an hourglass deformity is responsible for most of the symptoms.

5. The diagnosis is made by cystoscopy. The most distinguishing cystoscopic characteristics are the thick margin of the opening between the two cavities, the occurrence of normal bladder markings in the upper as well as the lower cavity, and a total bladder volume that is apparently unchanged from the normal. The ureters may open either above or below the constriction. Cystoscopically, the condition must be distinguished from other hourglass deformities, mainly from those due to diverticula. The diagnosis is substantiated at operation where the two cavities are seen to have walls of equal thickness which are normally constituted, and a constriction ring which is generally twice the thickness of the bladder wall.

6. Since the total bladder volume is apparently unchanged from that of a normal bladder, it is generally best to follow some procedure concerned with the eradication of the fibrous ring, whether the ureters open into the upper or into the lower cavity.

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Treatment.—Because of the severe infection in the bladder, a suprapubic cystotomy was done. The upper cavity was first entered. The cavities appeared about equal in size. Examination showed that the fibrous ring was extremely tough and very thick and was at least twice the thickness of the bladder wall. The opening was about 2 cm. in diameter. The walls of both cavities were found to be of equal thickness and presented similar layers and appearance. Considerable cystitis was found. Examination of the lower cavity showed that the ureters opened into it in normal position and that there was a small pedunculated prostate present. The neck of the hourglass deformity was dissected out, making one large cavity out of the two. The incision was closed with drainage.



Fig. 1.—Air cystogram showing hourglass appearance of the bladder.

Twelve days later when the cystitis had subsided five large pieces of fibrous prostatic ring were resected with the McCarthy resectoscope. The suprapubic incision promptly healed, and the patient was dismissed from the hospital one week later.

Five years after the operation the patient reported that he had had no bladder trouble and that he was still practicing medicine.

SUMMARY

1. Congenital hourglass bladder is one of the rarer human anomalies, with a total of sixteen cases, including a case of our own, now recorded in the literature.

2. The exact etiological factor responsible in the embryo for the constriction which divides the bladder into two cavities like an hourglass is not known, but it may be due to one of the following, namely, an atavistic relationship to hourglass bladder normally found in some animals, the persistence of the ureteric membrane, or unequal growth of the two bladder anlagen.

Henle (1878)⁶ and Pastau and Testut⁷ described again the anastomosis between the deferential and spermatic vessels. Jarisch (1888)⁸ showed that the testis received its arterial supply from three sources: the internal spermatic (the main supply), the deferential, and the external spermatic arteries. He did not recognize any relationship of these vessels with the serotal system. Capurro (1901)⁹ studied the arterial anastomoses of the testis in the dog by injecting gelatin into the internal spermatic artery through the aorta. Colle (1902)¹⁰ confirmed the rich anastomosis and in addition showed that the serotal vessels of both sides communicated across the midline and anastomosed with the external spermatic branches. Piequé and Worms (1909)¹¹ injected the internal spermatic artery at its entrance into the spermatic cord, verified the foregoing observations, but were unable to find any communication between the serotal and testicular vessels. The cremasteric artery was sometimes found inside the cord structures and at other times outside. Under the latter circumstances it gradually found its way by oblique penetration of the various coats of the cord until it reached the inferior portion of the testis to anastomose with the deferential and epididymal branch of the spermatic artery. Several types of anastomosis were described by Piequé and Worms (Figs. 1, 2, and 3).

According to Piersol,¹² "the front and sides of the serotum are supplied by the anterior serotal branches from the deep and superficial external pudic arteries and the back and septum are supplied by the posterior serotal artery, a branch of the internal pudic. Free communication exists not only between the vessels of both sides across the midline but also between the anterior and posterior branches at the sides. The serotal arteries anastomose with twigs from the obturator and internal circumflex as well as from the cremasteric artery."

The evidence points to the cremasteric artery as the key vessel in the collateral circulation when all the vessels in the cord are tied off above the serotum, since it alone communicates with the serotal system on the one hand and the testicular system on the other (Fig. 4).

The venous circulations of the testis and epididymis were studied carefully by Haberer¹³ in 1898. He showed that the blood returns by four possible routes: (a) Blood from the testis, into the anterior and posterior portions of the pampiniform plexus; (b) upper two-thirds of the epididymis, to the anterior pampiniform plexus through the epididymal veins; (c) tail of epididymis, by the deferential vein into the venous plexus about the seminal vesicles; (d) coverings of testis and cord, by the external spermatic vein into the inferior epigastric vein.

Anastomoses between the veins occur only in the lower portion. According to Wangenstein,¹⁴ interruption of the veins in the pampiniform plexus below the anastomoses will interfere with the circulation in the testis more than ligation of the internal spermatic vein high in the extraperitoneal region.

THE VIABILITY OF THE TESTIS FOLLOWING COMPLETE SEVERANCE OF THE SPERMATIC CORD

HAROLD NEUHOF, M.D., AND WILLIAM H. MENCHER, M.D.
NEW YORK, N. Y.

(From the Surgical Service of Dr. Harold Neuhoof, Mt. Sinai Hospital)

OWING to a recent opportunity to examine microscopically a testis whose spermatic cord had been severed, we are no longer in doubt concerning our observations on viability of the testis after deliberately performed section of the structures of the cord. Until this opportunity had been vouchsafed, we hesitated to report clinical observations which had been made over a period of years and whose presentation is the main purpose of this paper. In addition, the literature on the subject will be reviewed, the blood supply and collateral circulation of the testis will be discussed, experimental observations of others will be analyzed, and an explanation will be offered for the variation in results after complete severance of the cord.

Despite its clinical importance, there is no unanimity of view as to the effect of complete severance of the structures of the cord on the testis. Although the literature on the subject is scanty, it appears to have been generally assumed and accepted that the results range from partial or complete atrophy to gangrene. For example, Lower¹ states that, following the division of the entire cord in direct inguinal hernioplasty, "in all cases there has been very marked atrophy after a period of time." Eisendrath and Rolnick² observed that "ligation or division of the entire spermatic cord results in complete atrophy of the testicle and very often gangrene." On the other hand, Burdick and Higenbotham,³ in a report on severance of the cord in a large number of hernioplasties, observed that "many of the testicles atrophied but it was surprising how many did not." Although a statistical analysis of the results in their cases was not made, at least the fact that atrophy did not occur uniformly should be stressed as an experience at variance with a generally or widely held view.

In contrast to the scanty clinical contributions to the subject, considerable anatomical and experimental literature is available. The data which this literature contains will now be presented.

ANATOMICAL CONSIDERATIONS

According to Luschka (1863),⁴ the spermatic artery carries the sole blood supply of the testis. He recognized the existence of an epididymal branch but did not speak of its anastomosis with the deferential artery. Sappey (1873)⁵ was the first to recognize such an anastomosis. Later,

EXPERIMENTAL AND CLINICAL OBSERVATIONS

The blood supply of the testis and epididymis in dogs was found to be similar to that in man by a number of investigators (Ludwig and Tomsa,¹⁵ Griffiths,¹⁶ Ellenberger and Baun,¹⁷ Waugensteen¹⁴). Practically all of the experimental work on this subject was done on dogs; the results have been interpreted as being applicable to man.

Cooper (1845)¹⁸ was the first to study the effect of ligation of the vessels of the spermatic cord. On one occasion he divided between ligatures the whole of the spermatic cord. Sloughing and gangrene of the testis took place and he was content apparently with the result of this single experiment. Miflet (1879)¹⁹ showed that obliteration of the internal spermatic artery in dogs was followed by hemorrhagic infarction of the testis and that ligation of the internal spermatic veins alone

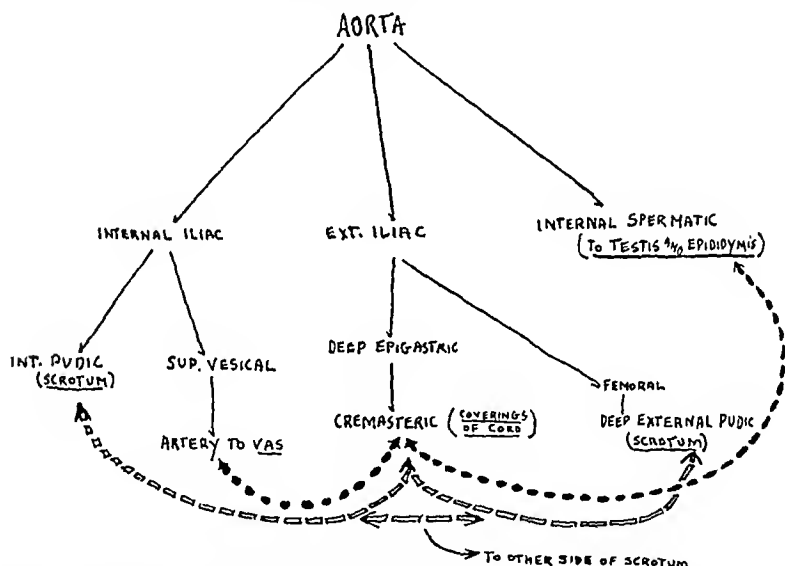


Fig. 4.—Schematic outline showing the cremasteric artery to be the key vessel between the testiculocremasteric-deferential-arterial system on the one hand and the scrotal-arterial system on the other.

was sufficient to cause degeneration of the testicular parenchyma. Thus, hemorrhagic infarction of the body of the testis followed by atrophy of the gland resulted whether the artery or the vein was ligated. However, Kocher (1887),²⁰ Treves (1891),²¹ and Bennett (1893)²² found that obliteration of the internal spermatic artery and veins caused neither sloughing nor atrophy. While changes may be produced in dogs by interference with the blood supply, long sections of pampiniform plexus with the spermatic artery may be removed for varicocele in man with impunity. Griffiths (1895),¹⁶ as a result of experiments on dogs, reverted to the older view. He observed that "1. Ligation of the spermatic artery in full grown dogs leads within a few days to great diminution in the bulk of the testis, caused by rapid destruction from degenera-

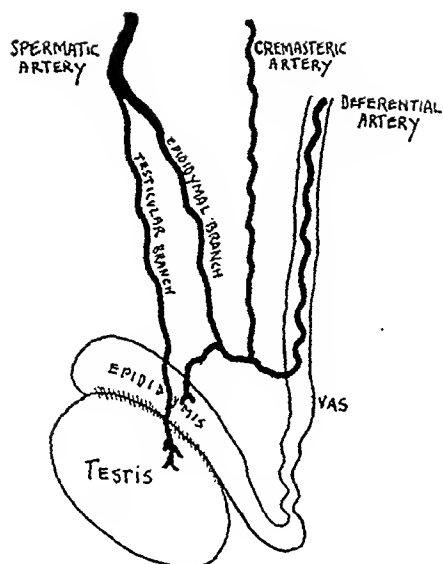


Fig. 1.—Showing anastomosis between the epididymal branch of the spermatic artery with the cremasteric and deferential arteries. (After Picqué and Worms.)

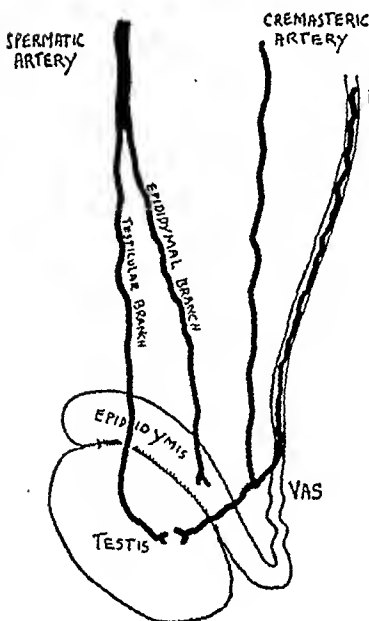


Fig. 2.

Fig. 2.—Showing anastomosis between the testicular branch of the spermatic artery and a branch from the cremasteric-deferential system. (After Picqué and Worms.)

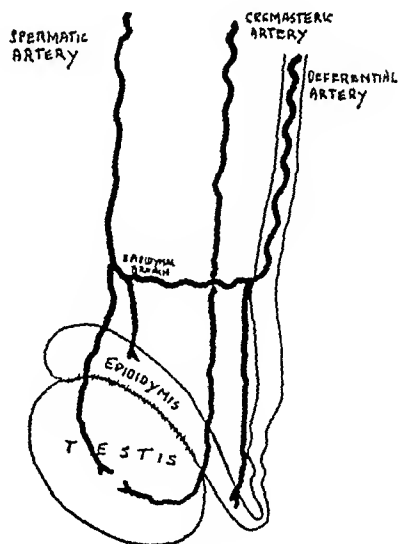


Fig. 3.

Fig. 3.—Showing double anastomosis: (1) between the testicular branch of the spermatic artery and the cremasteric artery; (2) between the epididymal branch of the spermatic artery and the deferential artery. (After Picqué and Worms.)

periments in dogs, noted that the tunica of the testis was thicker and more unyielding than that covering the epididymis and that tension in the testis was greater than that in the epididymis. Comparable pressure disturbances might take place in the testis after ligation of the vessels. He suggested that incisions through the tunica albuginea or a bisection of the testis with orchidorrhaphy might prevent atrophy. Incidentally, he confirmed, in a general way, the three types of anastomoses described by Picqué and Worms and demonstrated anew that the spermatic system communicated with the scrotal vessels and that the latter were noted to communicate with each other across the raphe.

Ligation or Division of the Vas Deferens.—The procedure of vasectomy dates from 1845 when Cooper reported unilateral vasectomy in a dog. Six years later an examination showed that the epididymis was distended with spermatozoa. Gosselin²⁹ performed vasectomy in two dogs. He found the testes normal six and ten months later. Curling (1866)³⁰ reported four experiments of vasoligation in which sperm was found abundantly present after two to eight months.

Concerning changes in the testis, Spangaro³¹ in 1903 was able to demonstrate spermatozoa in the testes but seemed surprised that no degeneration of testicular substance had been produced. Gregg³² found the testes perfectly normal four years after accidental vasoligation at an operation for hernia. Wallace³³ concluded from experiments on dogs that there is some distention of the epididymis following vasoligation and no dilatation of the tubules and that the growth of the testis and its function of producing spermatozoa are independent of the integrity of the vas. Oslund,³⁴ experimenting on dogs, concluded that vasectomy does not cause degeneration of germinal epithelium of the testis, and Moore and Oslund³⁵ concluded from their experiments on sheep that vasoligation does not result in degeneration of the epithelium of the seminiferous tubules. Wangenstein, experimenting with dogs, found no significant change in the testis after vas ligation. The conclusions seem to be uniform, therefore, that no injury to the testis or epididymis follows vas ligation or vasectomy.

CLINICAL EXPERIENCES WITH SEVERANCE OF THE SPERMATIC CORD

It is to be emphasized that most of the experimental work on dogs was confined to ligation or division of only some of the structures of the spermatic cord. We are concerned in this paper with the results of complete cord severance. The literature on this subject is scanty. Despite disagreement as to the effect on the testis of experimental ligation of part of its blood supply, the clinical observations after ligation or division of the entire spermatic cord in man seem to us to serve as fair indicators of the fate of the testis and the epididymis.

The procedure of complete severance of the cord structures has been employed by us to achieve complete hernioplastie closure in selected

tive changes in the seminal tubules; but, after a time the remaining tubules may recover to such a degree as to be capable again of producing spermatozoa in the usual way. 2. Ligation of all the spermatic veins leads to great swelling from engorgement of the veins and extravasation of blood into the intertubular connective tissues, and to necrosis of the epithelial cells in the seminal tubules. This condition would ultimately cause almost complete disappearance of the seminal tubules and atrophy of the gland. 3. Ligation of the spermatic artery and veins in puppies leads to great swelling of the testis and atrophy of the organs. 4. Ligation of the spermatic artery and veins in full grown dogs may lead to sloughing of the testis, complete atrophy and temporary fatty degeneration of spermatogenic cells in the seminal tubules which may be followed by complete recovery."

In 1902 Mignon²³ advocated section of all the vessels in the spermatic cord with the exception of those accompanying the vas deferens, as a measure to aid in the placement of the maldescended testis in the scrotum. Bevan (1903)²⁴ concluded independently from operations on varicocele, in which he had sacrificed all the vessels of the spermatic cord except those accompanying the vas, and in which no apparent interference with the testicular nutrition had occurred, that these vessels "could be safely sacrificed in those cases where it was necessary to divide them in order to bring the testicle well down in the scrotum." Moseheowitz (1910)²⁵ divided the spermatic vessels in dogs and removed the testis at periods varying from four days to three weeks after operation. In no instance did gangrene occur. Microscopically, some necrosis in the interior of the testis was noted occasionally, but the alveoli showed some degree of preservation in the periphery. Gessner,²⁶ operating according to Bevan on dogs (that is, division of all structures of the cord, except the vas, its artery and veins), found testicular atrophy in four out of five dogs, and therefore argues against avoidable division of the vessels of the cord. However, the section apparently was made in the scrotum. Mixer (1924)²⁷ found it necessary to divide the internal spermatic vessels in 15 out of 107 cases of undescended testes. Atrophy followed in all but 2 of these cases. Wangenstein (1927)¹⁴ showed that "section of the internal spermatic artery is followed always by diminution in the size of the dog's testis and by scattered degenerative changes in the tubules; spermatogenesis, however, still continues. Ligation of the internal spermatic artery with either the anterior or the posterior group of veins of the pampiniform plexus is followed by the same change that accompanies ligation of the artery alone. Ligation of the spermatic artery and all the veins in the pampiniform plexus always results in the total destruction of the testis."

It has been observed (Miffler, Wangenstein, and Joranson) that, while the testis atrophied, the epididymis remained normal. In seeking an explanation for this occurrence, Joranson (1928),²⁸ by perfusion ex-

In view of the fact that cord severance was performed only in those instances of hernioplasty in which recurrence was anticipated without complete closure of the canal, the incidence of 2 recurrences among 19 followed cases should be mentioned.



Fig. 6.—Low-power magnification of a portion of the resected testis (for description see text).



Fig. 7.—High-power magnification of a seminiferous tubule of the resected testis (for description see text).

Thus, in the study of this series of cases it is evident that retention of form and consistency of the testis occurred in the majority of cases so far as clinical observation was concerned. A recent opportunity to make a microscopic study of the testis in a case in which the structures of the

cases. However, there was one case (Case 10), in which severance of the entire cord was performed because a fibrosarcomatous tumor of the abdominal wall had involved the cord structures. There were 25 cases in which severance of the cord was employed. It was performed on one side only in all cases. There was no mortality. Eliminating 5 cases lost to follow-up or inadequately followed and 1 case in which orchidectomy was performed soon after operation (Case 13), there remain 19 cases for consideration. The follow-up varied from eight to fifty-five



Fig. 5.—The resected testis, epididymis, and spermatic cord.

months in these 19 cases. In 6 cases there was obvious atrophy of the testis (32 per cent); in 2 cases there was slight atrophy (10 per cent); and in the remaining 11 cases the testis, according to clinical observation of size and consistency, remained normal (57 per cent). There were, therefore, 13 cases in which little or no atrophy occurred (68 per cent). One case (A. H.) referred to above required orchidectomy soon after operation because of a dissecting hematoma which was due to an error in technique and is not ascribable to the severance of the cord.

| No. | G. L. (No.) | Age | History | Operation | Pathology | Result | Remarks |
|-----|--------------------|-----|---|---|---|---|---------------------------------|
| 9 | G. L. (No. 386966) | 52 | 2 yr. ago left hernioplasty; recurrence in 3 mo. | Direct-indirect left hernia | Hernioplasty; division of left cord (11/35) | O. K. | 12 mo. |
| 10 | A. C. (No. 362630) | 42 | 6 mo. mass in right inguinal region | Fibrosarcoma of abdominal wall | Removal of tumor and division of right cord (2/13/34) | Right two-thirds size of left | 36 mo. |
| 11 | P. R. | 38 | 4/35, left hernioplasty; recurrence in 3 mo. | Left recurrent inguinal hernia | Hernioplasty and division of left cord (7/35) | One-third size of right | 19 mo. |
| 12 | S. S. (No. 374084) | 51 | Bilateral inguinal hernia; small left sac, large right sac | Bilateral inguinal hernia | Bilateral inguinal hernioplasty; division of right cord (11/28/34) | Right O. K.; recurrent 3 mo.; no left, no | 27 mo. |
| 13 | A. H. (No. 371891) | 57 | 10 yr. ago right inguinal hernioplasty; recurrence 7 yr. ago | Recurrent right inguinal hernia | Hernioplasty; division of right cord (10/8/34); postoperatively; hematoma in wound and scrotum; destruction of testis | Orchiectomy | None |
| 14 | A. M. (No. 350209) | 75 | 30 yr. ago, right hernioplasty; 10 yr. ago recurrence; 1933 right hernioplasty for recurrence; 2 mo. ago left inguinal hernia | Left inguinal hernia (direct-indirect) | Hernioplasty; division of left cord (10/2/34); postoperatively; left cord became thickened to 2 cm. | O. K. | Small recurrence (right) 28 mo. |
| 15 | J. S. (No. 375162) | 42 | Bilateral hernias several year ago | Large direct-indirect on right; small on left | Bilateral hernioplasty; division of right cord (12/34) | Atrophy | No |
| 16 | B. M. (No. 381374) | 42 | 6 mo. bulge on right side | Bilateral hernia | Bilateral hernioplasty; division of right cord (6/24/35) | O. K. | 12 mo. |
| 17 | B. H. (No. 390380) | 43 | 1933 hernioplasty for ventral hernia | Left indirect inguino-scrotal hernia | Hernioplasty; division of left cord (2/36) | O. K. | No |

TABLE I

| CASE NUMBER | NAME | AGE | HISTORY | DIAGNOSIS | OPERATION | DATE OF TESTIS | RECURRENT OF HERNIA | PERIOD OF FOLLOW-UP |
|-------------|--------------------|-----|--|---|---|----------------------------|---------------------|---|
| 1 | S. K. (No. 366333) | 43 | Left hernia 2 yr. duration | Left direct hernia | Hernioplasty and division of left cord (5/17/34) | One-half atrophy | No | 13 mo. |
| 2 | N. T. (No. 394054) | 33 | Swelling in left inguinal region 1 wk. | Right recurrent inguinal hernia | Hernioplasty; right cord divided (6/36) | Atrophy | No | 11 mo. |
| 3 | J. B. (No. 393461) | 45 | Lump in right groin 15 yr. duration | Right direct and indirect scrotal hernia | Hernioplasty; right cord divided (6/36) | O. K. | No | 25 mo. |
| 4 | S. C. (No. 397880) | 45 | Hernioplasty 1 yr. ago; recurrence soon after operation | Right recurrent inguinal hernia | Hernioplasty; right cord divided (9/36) | Little smaller in size | No | 8 mo. |
| 5 | H. G. (No. 383921) | 50 | Swellings in both inguinal regions for several years | Bilateral hernia | Bilateral hernioplasty; left cord divided (8/29/35); reaction right cord and testis postoperatively | Left O. K. | ? | |
| 6 | J. L. (No. 396380) | 45 | 8 yr. ago right inguinal hernioplasty; recurrence in 6 mo. | Irreducible right recurrent inguinal hernia | Hernioplasty; division of right cord (7/36) | O. K. | No | 26 mo. |
| 7 | A. S. (No. 377304) | 57 | Right inguinal hernioplasty 7 yr. ago; recurrence in 2 yr. | Right recurrent irreducible direct-indirect inguinoscrotal hernia | Hernioplasty; right cord divided (3/5/35) | O. K.; right testis larger | No | 55 mo. |
| 8 | H. C. (No. 393801) | 20 | Right hernioplasty 3 yr. ago; recurrence in 7 mo. | Recurrent inguinal hernia | Hernioplasty; right cord divided (5/29/36) | O. K. | No | 31 mo. later, orchidectomy for suspected neoplasm; microscopic examination showed essentially normal testis |

cord were severed thirty-one months before offered clinching evidence to support the clinical impression of testicular viability. This case (H. C., Case 8) warrants special presentation.

CASE REPORT.—The patient was a man 20 years old in whom a right hernioplasty was performed three years previously. There was a recurrence of the hernia within seven months. On May 29, 1936, hernioplasty was performed for the recurrence and the whole right spermatic cord was severed in order to effect tight closure. There has been no recurrence of the hernia. The recent development of swelling and a sense of a mass in the right testis led to its removal for suspected neoplasm thirty-one months after the cord structures were severed. At operation the spermatic cord was exposed and no pulsation could be felt in the spermatic artery. The testis, epididymis, and vas up to the external ring were removed.

Gross Pathologic Description.—"Specimens consisted of a resected testis and epididymis and 8 cm. of the spermatic cord. Upon opening the tunica vaginalis there was revealed a testis normal in size and shape, measuring 4.5 by 3.5 by 2.3 cm. The epididymis also appeared normal in size and shape. On section, the body of the testis presented a tawny cut surface which was somewhat edematous. The tubules could be strung with ease. No areas of atrophy or fibrosis were evident. Section through the epididymis disclosed nothing unusual. The structures of the spermatic cord presented no abnormalities." (Fig. 5.)

Microscopic Description.—(Figs. 6 and 7.) "The seminiferous tubules appeared somewhat reduced in number and rather widely separated from each other, as though by edema of the interstitial tissue. However, there were no fibrous or hyaline tubules such as one sees in the usual areas of tubular atrophy in the testis. Many of the tubules appeared somewhat dilated. This appearance is enhanced by a reduction in the cells of the tubules. All stages of spermatogenesis were observed, although the sum total was reduced. In addition to this quantitative variation from normal there were certain qualitative aberrations. In some tubules complete inactivity was evident. In others there seemed to be some abnormality in the transformation of spermatids into mature spermatozoa. The latter lacked for the most part the usual elongated spearheads. The heads appeared, instead, round. Tails were not found. This may have been due to inadequate fixation. Some of the tubules contained a homogenous, basophilic coagulum. The number, appearance, and distribution of the interstitial cells were normal. The blood vessels were unchanged. The structures of the epididymis were not unusual. A few tubuli epididymides contained small numbers of round-headed spermatozoa whose tails could not be distinguished."

This case is unique in that we were able to study microscopically for the first time the late effect of complete severance of the spermatic cord (almost three years after the operation). The findings prove that the testis was only insignificantly altered following complete division of the cord.

TECHNIQUE OF OPERATION

The technique of severance of the cord is simple. Each structure is tied off by separate suture. Mass ligatures are not employed. The cord should be tied off above the scrotum, between the external and the internal abdominal rings. Ligature of the cord structures in the scrotum, at or below the external ring, destroys any possible collateral anastomosis. It is evident that meticulous aseptic and hemostatic technique is

TABLE I—CONT'D

| CASE NUMBER | NAME | AGE | HISTORY | DIAGNOSIS | OPERATION | FATE OF TESTIS | RECU- RENCE OF HERNIA | PERIOD OF FOLLOW-UP |
|-------------|-----------------------|-----|---|--|---|---|-----------------------------|------------------------|
| 18 | L. S. (No. 395466) | 56 | Right hernia, 20 yr.; left hernia, 5 yr. | Bilateral inguinal her- nia | Bilateral hernioplasty 2 stages; division right cord (3/10/36) | Right epididy- mis thick- ened; testis O. K. | No | 24 mo. |
| 19 | R. G. (No. 397303) | 56 | Right inguinal swelling about 1 yr. | Right direct-indirect hernia | Hernioplasty; right cord divided (8/36) | O. K. | No | 24 mo. |
| 20 | J. W. (No. 403085) | 47 | Lump in right scrotum 5 mo. | Right scrotal hernia | Hernioplasty; right cord divided | ? | ? | |
| 21 | J. Z. (No. 403204) | 47 | 5 yr. bulge in left groin | Left indirect inguinal hernia | Hernioplasty; left cord divided (1/6/37); postoperative reaction in cord | Atrophy and thickening | No | 11 mo. |
| 22 | J. M. (No. 382647) | 55 | 8 mo. bulge in left groin | Left indirect inguinal scrotal hernia | Left hernioplasty; left cord divided (7/27/37) | | | 16 mo. |
| 23 | J. B. (No. 383425) | 51 | Lump in right groin for many years held in place by truss; re- cent occasional irre- ducibility | Right direct-indirect hernia (inguinal) | 8/17/35 | O. K. | No | |
| 24 | J. G. (No. 404118) | 39 | 1915, induced hernia; 3 hernioplasties with recurrences | Recurrent direct-indi- rect inguinal hernia | Left hernioplasty; left cord divided (2/5/37) | Atrophy on e- third size | No | 14 mo. |
| 25 | G. M. (No. 437062) | 37 | Lump in right groin and scrotum, 3 yr. | Sliding hernia of cecum | Right hernioplasty; di- vision of right cord structures (3/6/39); postoperative testicu- lar swelling and in- fection of wound | ? | No | 6 mo. |

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required, otherwise a resultant hematoma dissecting along planes into the serotum will interfere by compression with the collateral circulation. Infection may lead to the same result if the serotum becomes involved. Should there be any indication of hemorrhage or infection, immediate opening of the entire wound and evacuation of the dissecting clot or pus is necessary in order to relieve compression of collateral vessels.

A study of our cases demonstrates that there is little or no apparent effect upon the testis and the epididymis in the majority of cases if a careful technique is employed. A maldescended testis is variable and displaced, and severance at any point might interfere with the collateral circulation.

SUMMARY

1. The testiculoepididymoscrotal arterial and venous systems comprise a potential collateral circulation for the testis in case of complete severance of the structures of the cord in the inguinal canal.

2. The severance of all the structures of the cord in 24 cases resulted in no immediately obvious abnormality in the testis.

3. In an adequate follow-up of 19 of these patients over a period of eight to fifty-five months, very little or no atrophy was observable in 13 patients (68 per cent) and obvious atrophy in 6 patients (32 per cent).

4. Microscopic study of the testis removed in one of these cases thirty-one months after complete severance of the structures of the cord revealed an essentially normal testis.

5. A careful aseptic and hemostatic technique is an essential factor in safeguarding the development of a collateral circulation, and thus preserving the testis in the majority of cases.

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appear to be of critical importance. Even if it could be established that genu valgum is the invariable sequel of the operation, the condition is so readily amenable to correction by supracondylar linear osteotomy that it should not be urged as a valid contraindication to the operative intervention, provided the intervention were otherwise satisfactory.

By far a more serious objection, and undoubtedly the one which accounts for the lack of popularity of the operation, is the interference in mobility which, in varying degrees, has been observed almost routinely. It is this disability which forms the main theme of the present communication. Before proceeding to its consideration, a third objection, not previously stressed, should be noted.

Because of the satisfactory results obtained in adults, the indications for the operation have been extended to include the treatment of similar conditions in children. However, experience soon showed that, even in the hands of the same surgeon, the response of children to the bifurcation procedure might be entirely different from that seen in adults. In the latter, the shape given to the femur could, with confidence, be expected to remain unchanged. In children, on the contrary, it was observed that even in cases in which "ideal" bifurcation had been performed, the "spike" of the distal fragment tended to disappear. The femur gradually lost its given configuration and with the lapse of time assumed a form reminiscent of that obtained after a Schanz type of osteotomy.⁶ Although this was explained as an inherent response of growing bone to the altered stresses occasioned by the osteotomy, the disappearance of the projecting and presumably supporting upper end of the distal fragment was disconcerting. Indeed, it almost seemed to contraindicate the use of the operation in children.

But even this did not seem to exhaust the difficulties which these patients presented. Further observation recalled almost paradoxically that, while instability might be the consequence of a loss of the bifurcation configuration, pain and limitation of motion persisted in certain cases in which the bifurcation was not lost.

CASE 1.—Marjorie G., aged 6 years, was seen in the Outpatient Department in June, 1932, with a history of a peculiar gait since the age of 2. Examination disclosed a bilateral congenital dislocation, with all the classical signs and symptoms. Because of the fact that the acetabular fossae seemed to be largely replaced by bone reposition, simple reduction was deemed inadvisable, and anterior transposition, after preliminary traction, was decided upon. By means of Hoke traction, the femoral heads were pulled down to about the acetabular level. Adduction tenotomy was performed, and anterior displacement of the femoral heads was undertaken. Although it appeared to have been successfully carried out, the result as to stability was not considered satisfactory. The patient was consequently readmitted to the hospital, and bifurcation was performed on the left hip in January and on the right hip in March, 1934. The convalescence was of a routine nature, and the patient was discharged from the hospital in April, 1934. In June, 1934, it was noted that internal rotation was limited, that adduction was painful, and that flexion, which was limited, occurred only on external rotation. The

THE BIFURCATION OPERATION

HENRY MILCH, M.D., NEW YORK, N. Y.

(From the Hospital for Joint Diseases, Service of Dr. Harry Finkelstein)

THE operative procedure which has become known as the "bifurcation" operation was apparently first described by Lorenz,⁵ although he admitted the similarity in principle of this operation to other types of subtrochanteric osteotomy used by Kirrnisson⁴ and previous to that by other American surgeons. Lorenz was of the opinion that special merit accrued to the particular osteotomy which he recommended. Originally suggested by the observation of a pseudoarthrosis of the femoral neck, the rationale of its application to other conditions, and especially to the treatment of irreducible dislocations of the head of the femur, was quickly recognized. In addition, it has been recommended in a number of different conditions: upward dislocation of the femoral shaft following a destructive epiphysitis, fractures of the acetabulum, nonunited fractures of the femoral neck, and the painful coxarthritides in which ankylosis has not occurred.^{1, 2}

In essence, the operation constitutes an effort to divert the stream of body weight, so as to restore stability without sacrifice of hip joint mobility. Although the procedure makes no attempt at restoration, either of normal anatomy or physiology of the injured hip joint, there is no doubt that it does succeed, in many cases, in rehabilitating the functionally incapacitated patient. It is a relatively simple technical procedure, which can be quickly performed, with but little shock. It actually does re-establish stability in the unstable hip joint. It relieves pain and permits of at least partial physiologic rest to an inflamed or otherwise irritated joint.

It would seem to be exactly the sort of operative intervention which should have fired the imagination of the orthopedic surgeon. This is not the case. With the exception of some few who insist upon its merits, the procedure does not seem to have won general popularity. It is interesting to note that it is particularly in the treatment of the unreduced, congenital dislocations, for which the operation was originally recommended, that the greatest dissatisfaction has been manifested.

In the main, the objections have been twofold. The first of these is concerned with the apparent development of a postoperative knock-knee. Although some have claimed, and quite reasonably, that the abducted position of the distal portion of the femur predisposes to the formation of a genu valgum, others have insisted that this was merely apparent, or was present before operation. This moot point can be readily determined by pre- and postoperative axial measurements and does not

tory" bifurcation. Since by far the greater majority of the bifurcation operations had been performed for unilateral indications, the disability did not appear to be sufficient to justify the casual discard of the procedure. Although the patient's complaints of pain could not be entirely disregarded, they were accepted as representing the price paid for the acquisition of stability by means of a relatively simple operative intervention. It was only when a review of the bilateral bifurcations was undertaken that the extent of the disability was fully appreciated and a clue to its causation was found.

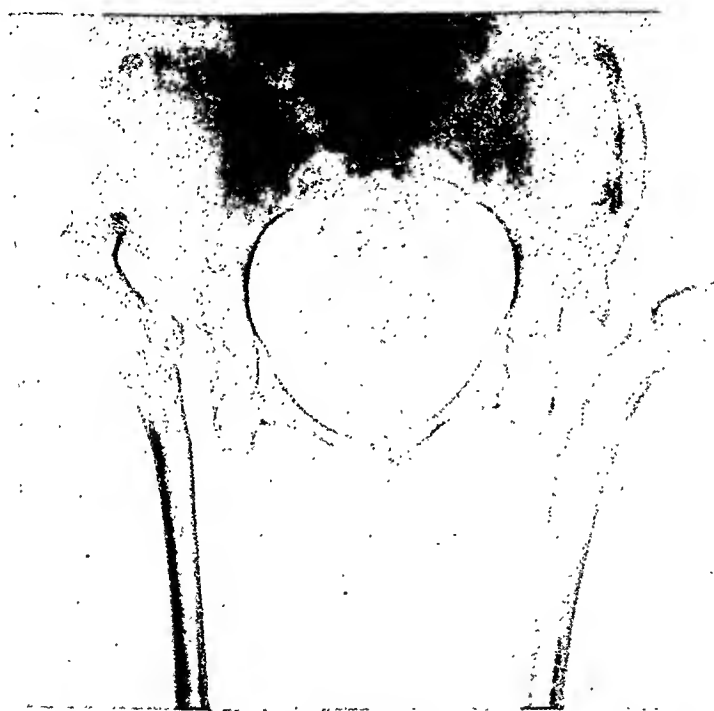


Fig. 2.—Case 1. Roentgenogram made in February, 1937. The angle of the upper end of the right femur is approximately that of the pelvic wall. On the left side, the angle is definitely less.

A strikingly similar clinical picture was discovered in all. There was an annoying increase in the intercrural distance, with an inability to bring the legs into parallelism. The patients could not completely flex or adduct the thighs. In the seated position they could not cross their legs tailor-fashion. They could not assume the squatting position and had difficulty in putting on their shoes or stockings. In the erect position, they stood with the legs abducted and the feet everted. Forward progress was possible only with a peculiar twisting and waddling gait. Nevertheless, the Trendelenburg sign was invariably negative. Pain was present in varying degree. In some patients the pain was so mild that it was overlooked in their satisfaction at the restoration

roentgenogram (Fig. 1) taken in August, 1934, showed what appeared to be Schanz osteotomies performed at different levels. In November it was noted that the child complained of pain and walked with a peculiar waddling gait. Because the Trendelenburg sign was negative, the waddle was attributed to fear and muscle weakness.

As time went on it was noted that on the right side pain and the waddle persisted. On the left side these disappeared with recurrence of instability. In February, 1937, the roentgenogram (Fig. 2) disclosed a loss of the typical configuration on the left side, with its persistence on the right.



Fig. 1.—Case 1. Roentgenogram made in August, 1934, after bilateral osteotomy.

Because of the firm belief in the necessity for pelvic support, the pain and limitation of motion on the one side, at the time, was unfortunately overlooked. Interest centered mainly on the other side, and the apparently bizarre outcome was accepted, without more ado, as another one of the bifurcation peculiarities which had been observed repeatedly in adults. In many adult cases in which "unsatisfactory" bifurcation had been performed, the functional result was frequently excellent, although the roentgenographic appearance left much to be desired. Instead of bifurcation, osteotomy, either at a high or a low level, had been performed. Even where the osteotomized fragment made no contact with the pelvis, stability had been restored, without any material limitation of motion. Yet, strange to relate, it was frequently noted that the greatest disability appeared precisely in those very cases which presented the most typical roentgenographic evidence of anatomically "satisfac-

at the age of 12 years. She presented all the pathognomonic signs of bilateral hip dislocation. This was confirmed by roentgenographic examination. Because of the high position of the femoral heads, preliminary skin traction, and later skeletal traction, was attempted, but without success. In 1933 adductor tenotomy and then anterior transposition of the femoral heads were carried out to balance the pelvis and overcome the marked lumbar lordosis. The roentgenogram showed the position of the femoral heads beneath the anterior iliac spines. The results of this transposition were not satisfactory, and bifurcation was recommended to overcome the waddle and establish stability.

In November, 1933, bifurcation was performed on the right side. In January, 1934, bifurcation was performed on the left side (Fig. 3). In both instances the effort was made to place the upper end of the distal fragments into the acetabula, according to the precepts of Lorenz and of Haas.³ On the left this was accomplished but on the right side the effort failed. In March, 1935, it was found that both bifurcations had lost their characteristic appearance and had assumed almost their preoperative appearance (Fig. 4).

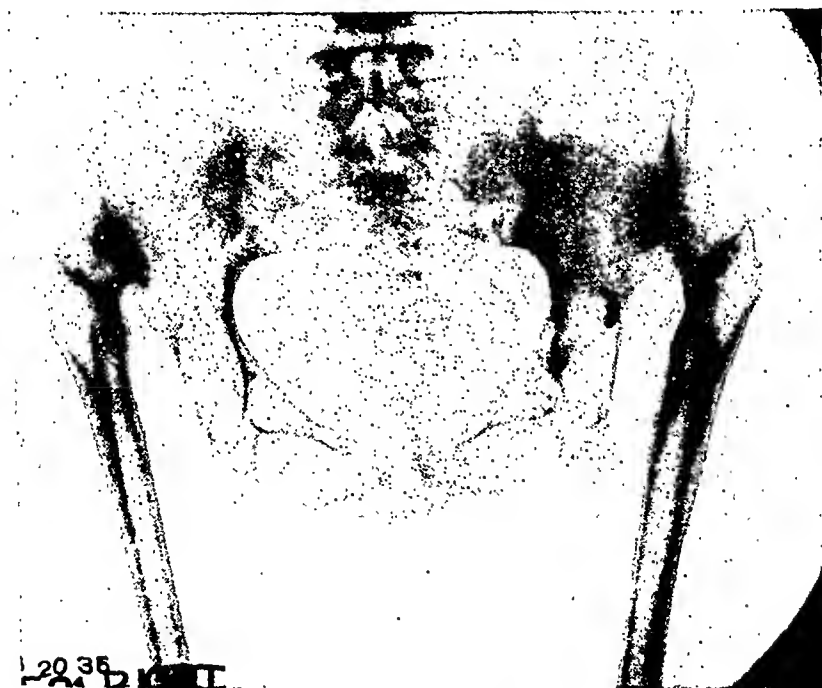


Fig. 4.—Case 2. March, 1935. The bifurcation has disappeared. It is barely possible to recognize that osteotomy has been performed.

Because of the persistence of the waddling gait, operative revision of the bifurcation was advised. This was performed on the left side in October and on the right side in December, 1935. A roentgenogram taken in April, 1936 (Fig. 5) showed good bilateral bifurcation. It is to be noted that the anatomic appearance on the right side is almost that of a Schanz osteotomy. On the left side there is a well-formed spike, which is placed directly in the acetabulum, and the femoral head does not appear to be in close contact with the pelvic wall. Even after this revision, the result left much to be desired. In 1938 the patient still walked with a peculiar twisting waddle. She was unable to cross her legs or to

of stability. In others, it was so severe that the patients insisted on relief, even at the risk of reoperation.

In these cases one factor appeared to be constant. Roentgenographically, all showed good bifurcations, but in all a long spike, formed by the upper end of the osteotomized fragment, persisted. The obvious inference was that this was the cause of the difficulty; the obvious indication was for its removal. But, since the spike is of the very essence of the bifurcation operation, its removal seemed to imply a negation of the previous surgical effort. Without further consideration, this did not



Fig. 3.—Case 2. Roentgenogram made in February, 1931, after the first bilateral bifurcation operation.

seem warranted. It was at this stage that the experience with the bifurcation operation in children came to mind. As has already been noted, instances had been observed in which stability was preserved, despite the loss of the spike. It seemed, therefore, justifiable to reproduce, surgically, the effects which nature had demonstrated in children.

With this object in view, several patients were admitted to the hospital for the specific purpose of resecting the projecting spike of the distal osteotomized fragment. The two cases herewith recorded are typical.

CASE 2: *Bilateral bifurcation for congenital hip dislocations, with subsequent removal of persisting bone spike on left side.*—Mary M. was seen in July, 1932,

walk with the left foot pointing forward. There was moderate limitation of motion in all arcs of motion on the left side.

| | RIGHT | LEFT |
|-------------------|----------|------|
| Flexion | Complete | 90° |
| Extension | 175° | 180° |
| Abduction | 70° | 60° |
| External rotation | 60° | 50° |
| Internal rotation | 30° | 5° |

A roentgenogram (Fig. 6) taken in June, 1939, disclosed the startling explanation of these phenomena. On the right side the bifurcation had again lost its characteristic form, but on the left the spike had persisted. Lateral views, not reproduced here, demonstrated the forward projection of this bony prominence.

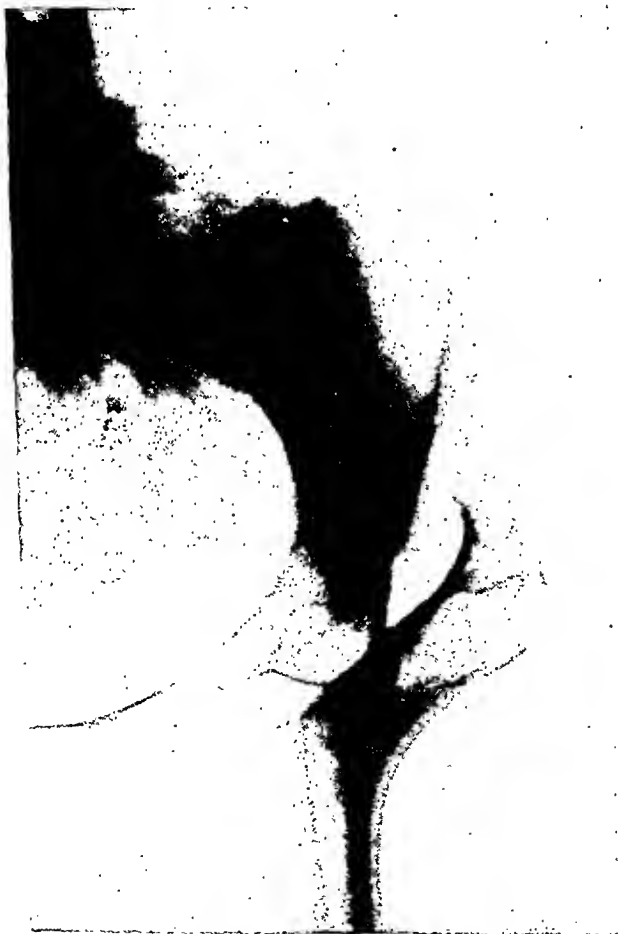


Fig. 7.—Case 2. July, 1939. The spike has been amputated, with prompt restoration of motion.

In the conviction that this was the cause of the patient's disability, resection of the bony block was advised and carried out in June, 1939. On the operating table it was clearly demonstrated that the limitation of internal rotation was caused by this spike, and that immediately upon its removal the limitation dis-

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Fig. 5.—Case 2. April, 1936. Roentgenogram made after second bilateral bifurcation.



Fig. 6.—Case 2. June, 1939. On the left side the bifurcation character has been preserved. The projecting spike, with the head, forms an angle greater than the angle of inclination of the pelvic wall.

walk with the left foot pointing forward. There was moderate limitation of motion in all arcs of motion on the left side.

| | RIGHT | LEFT |
|-------------------|----------|------|
| Flexion | Complete | 90° |
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appeared. The patient's convalescence was uneventful, and she was permitted out of bed as soon as the soft tissue wound had healed. Even as early as several weeks after operation, the patient showed a marked improvement in gait. The stability was well preserved, and, bearing her full weight, the patient was able actively to rotate her left leg internally to 20° . Forward progression was possible in a normal manner, with only a slight limp and pelvic tilt. The roentgenogram (Fig. 7) taken in July, 1939, revealed that the spike had been completely resected.

CASE 3: Bilateral congenital femoral dislocation treated by bifurcation and subsequent amputation of "spikes."—Emma S., aged 27 years, was seen in the Out-patient Department in March, 1937. There was a history of a limp, waddling gait, and difficulty in standing and walking since childhood. The recent appearance of pain in the hips forced the patient to seek medical assistance. Physical examination disclosed all the classical signs of a bilateral, congenital, femoral dislocation. An x-ray taken in March, 1937, showed "bilateral, congenital dislocation with [it is to be noted] adduction deformities of both femora. The newly



Fig. 8.—Case 3. April, 1938. Roentgenogram made after bilateral bifurcation. The angles of the upper end of the femur are obviously greater than the angle of pelvic inclination.

formed acetabulum on the right side shows marked, productive changes." In March, 1937, bifurcation of the left femur was performed in the oblique sagittal plane. The postoperative convalescence was uneventful, and in August, 1937, the patient was readmitted for a similar bifurcation of the right femur. The patient was discharged, walking with crutches, in November, 1937.

In January, 1938, the patient complained of severe pain in both groins. She noted that the right leg seemed longer than the left. She walked in a guarded manner, the right leg held in marked abduction and external rotation, with the knee in flexion. The left leg was in less marked abduction and external rotation.

As in the right leg, internal rotation was impossible, either passively or actively. The patient could not adduct her legs in standing or cross her legs in sitting. She was given physiotherapy and encouraged to discard her crutches, but without any subsequent improvement in gait or comfort. A roentgenogram taken in April, 1938, disclosed the reason for the disability; the upper ends of the distal fragments were found to abut anteriorly against the acetabular rim and not against the ischial tuberosity, as had been previously reported (Fig. 8).

The patient was readmitted to the hospital for the purpose of removing this abutment on the right side. At operation, the upper end of the distal fragment was found in contact with the pelvic wall, anterior to the acetabulum. Internal rotation of the femur was prevented by the bony prominence, even with the leg in abduction. The spike was partially removed, and immediately thereafter there was marked relief of pain in the right groin. The patient was able to flex the thigh, but only on abduction; the power of adduction improved, but internal rotation remained limited, probably because of insufficient removal of the bone spike. Following her discharge from the hospital, there was marked improvement noted in the gait, but she continued to complain of pain in the left groin.



Fig. 9.—Case 3. January, 1940. The spike has been largely amputated on the left side, with excellent restoration of function. On the right side partial amputation resulted in continued impairment of function.

In November, 1938, the patient was again admitted for operation on the left side. The spike of the distal arm of the bifurcation was found projecting forward into the thigh musculature. When an effort was made to bring the leg into the neutral position, the spike impinged against the side of the pelvis. From the experience gained at the previous operation, it was realized that a more liberal resection of the spike was necessary. Although complete removal of the bony projection was impossible, the result was more satisfactory than on the opposite side. There was an increased range of rotation and almost complete subsidence of the

pain. The postoperative roentgenogram of the left leg showed fairly satisfactory removal of the obstructing spike.

Upon her discharge from the hospital in December, 1938, the patient's right leg was still held in moderate abduction and external rotation. There was marked diminution in pain. The gait was greatly improved but was still unsightly, and the patient was unable to cross her legs when sitting. In January, 1940, a roentgenogram showed that, on the left side, the bifurcation had been converted into a modified Schanz osteotomy by removal of the spike. On the right side a truncated spike still persisted (Fig. 9).



Fig. 10.—Case 3. February, 1940. After secondary resection of the spike on the right side, the patient was able to bring both legs into parallelism, with marked restoration of mobility in all directions.

The patient was admitted to the hospital for the removal of this bony projection. The day following operation she was able to stand erect with her extremities parallel. Within two weeks the patient could cross her legs. In the erect position, the legs could be held together. Rotation, flexion, and abduction were almost normal. She walked with the feet pointing forward. There was still a slight waddle, but the twisting component had disappeared. The stability was excellent, and the Trendelenburg sign remained negative. The pain had completely subsided. The roentgenogram taken in February, 1940, showed marked reduction in the size of the projecting spike (Fig. 10).

The study of these and other cases established beyond question that, even in the hands of the same surgeon, the response of children to the bifurcation procedure was entirely different from that seen in adults. Whereas in adults the form given to the femur could with confidence be expected to remain essentially unchanged, in children it was found that with the lapse of time the given shape became so modified that the results observed shortly after operation differed radically from those noted at later examinations. During the early period, in children, stability was without exception restored. Where excessive abduction, unduly prominent spike formation, or improper double contact with the pelvis occurred, a marked impairment of gait and even painful limitation of motion were commonly seen. But almost invariably these unpleasant sequelae gradually disappeared as the children grew older. The pain subsided and the gait improved, but all too frequently the previously acquired stability vanished at the same time. When the roentgenographic series of these patients was examined, it was found that, as the stability disappeared, the femora manifested a typical sequence of variation. Beginning with the characteristic "Y" shape of the Lorenz bifurcation, the femur assumed the hockey-stick shape of the Schanz osteotomy and tended ultimately toward the original shape of the bone.

In the instances where this did not occur, it was found that, as in adults, pain and limitation of motion were invariably associated with excessive abduction or spike formation. In the unilateral cases, and in the erect position, this interference in motion is marked by tilting of the pelvis. The degree to which such compensation can occur is determined in large measure by the mobility in the opposite hip and the sacro-lumbar articulations. When seated, the possibility of pelvic tilt is precluded and the characteristic limitation of motion is readily demonstrable. These patients cannot cross their legs; they have difficulty in putting on shoes or stockings, and they cannot sit on low chairs. However, it is in the bilateral cases that the full extent of the disability becomes apparent. When the abduction of the distal fragment makes an angle with the femoral neck which is greater than the angle of inclination of the outer pelvic wall, these patients cannot bring the legs into parallelism for normal progression. As a result, the gait is awkward and may best be described as a twisting waddle, which persists despite a negative Trendelenburg sign. The feet are held everted, and rotation is markedly limited. In addition, the patients not infrequently are afflicted with such pain in the groin that they insist upon relief.

In children, the disability may disappear spontaneously as the upper end of the femur loses the appearance of bifurcation. Where this does not occur and where the spike persists, these young patients suffer the disturbances which are seen in their elders. In these the same tendency

toward loss of the bifurcation may be noted occasionally, but the rate at which this change occurs is relatively so slow that a more expeditious therapy must be instituted.

These disabilities can be promptly overcome by resection of the spike which is the hallmark of the bifurcation operation. The fact that this can be accomplished with restoration of mobility and without loss of stability seems to indicate clearly that the spike is not essential to the successful outcome of the osteotomy, and that, on the contrary, it is the cause of the undesirable effects almost routinely found after a typical bifurcation operation.

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THE APOPHYSEAL INTERVERTEBRAL JOINTS

ALBERT OPPENHEIMER, M.D., BEIRUT, SYRIA

(From the Department of Roentgenology, School of Medicine, American University of Beirut)

OBJECT OF STUDY

OF THE two forms of joints in the vertebral column, only the apophyseal joints, which connect the neural arches, are true diarthrodial articulations. They differ from the synchondroses formed by the disk and vertebral bodies almost as much as the hip joints from the pubic symphysis. In the pathology of the spine this difference is more important than is generally appreciated; it seems to have been recognized first by Fraenkel,⁵ in 1903, but its clinical significance is not yet fully known. Lesions of the apophyseal joints are not easily interpreted. The joints may be involved in various affections of the vertebral bone, but they may be affected independently by the different forms of arthritis, in which case other vertebral parts in turn may become involved. Hence, it is difficult to distinguish primary from secondary or incidental lesions. Reactions usually considered characteristic, such as osteophytes, rarefaction, calcification of ligaments, or destruction of cartilage, are common to many vertebral diseases and may develop after the primary lesion is healed. Since most vertebral diseases take a chronic course, post-mortem examination usually shows the multifarious consequences rather than the primary or essential features of the morbid condition. Relevant features, e.g., of arthritis, may thus escape verification. Within its own limits, roentgenologic study shows at least some of the stages of the pathologic process and reveals quite frequently the anatomical condition present at the time of the clinical examination. Correlations between anatomical and clinical findings can hardly be analyzed in another way. This report is concerned with the anatomical characters of the lesions involved, with their classification, and with the clinical manifestations observed.

RADIOGRAPHIC METHOD

As late as 1936 it was held that involvement of the apophyseal joints cannot be shown on radiographs.⁷ Methods of x-ray examination and significant findings were described for the lumbar spine in 1929,³ 1931,¹¹ and 1934;⁶ for the thoracic spine in 1934;¹³ and for the entire spinal column in 1938.¹⁷ The radiographic positions are determined by the angles which the joint spaces or the corresponding facets* form with the frontal plane: 90 degrees in the cervical section, nearly 20 degrees in

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*The terms apophyseal joint, articular process, and facets are often used synonymously. The facets are the bony surfaces of the articular process to which the cartilages of the apophyseal joint adhere. The apophyseal joints are often referred to as small, posterior, lateral, or intervertebral joints.

the dorsal section, and 45 degrees in the lumbar section (Fig. 1). The direction of the facets is constant in the cervical and thoracic regions, but it varies individually in the lumbar spine where the facets of caudal segments may be rotated forward more strongly than those of superjacent ones. This results in abnormal projections easily mistaken for morbid changes (Fig. 2). In the dorsal spine, where the articular processes are flat and slender and the joint spaces narrow, inaccurate technique results in pictures that cannot be interpreted (Fig. 2).

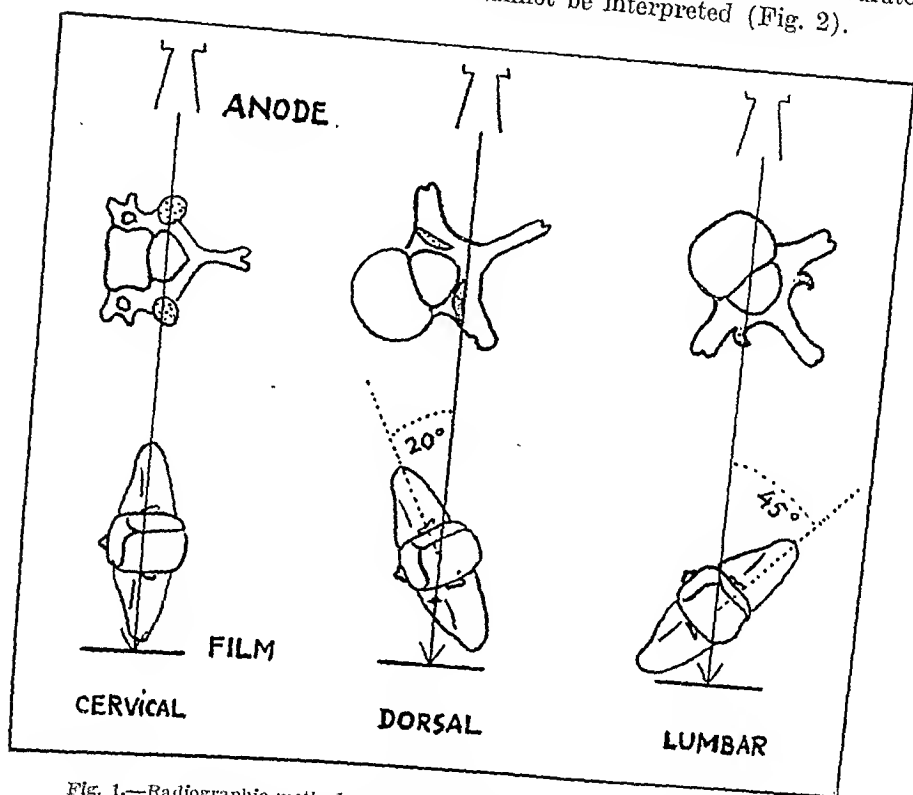


Fig. 1.—Radiographic method for demonstration of the apophyseal joints.

DEVELOPMENTAL VARIATIONS AND ANOMALIES

The articular processes may vary appreciably in size, shape, and position in the same segment; they are always broader and shorter in children than in adults (Fig. 3). In the newborn a radiolucent interspace, corresponding to the epiphyseal cartilage between vertebral body and neural arch, is seen slightly ventral of the apophyseal joint (Fig. 3). It ossifies usually in the course of the first five years. Gaps in the tips of the articular processes and in the isthmus or interarticular portion (Fig. 4) correspond to abnormally persistent cartilages separating bones which originate from distinct centers of ossification.^{1, 2, 4, 8, 10, 24} A peculiar supernumerary bone adjacent to a nonossified isthmus is shown in Fig. 4; this anomaly seems to have not yet been recorded. Hypoplasia

or complete absence of articular processes is rather common when combined with other developmental disorders, but it is rare as an independent occurrence (Fig. 3). The articular processes of block vertebrae may be fused. Synostosis of the articular processes only is not uncommon in the upper cervical segments (Fig. 3). A supernumerary apophyseal

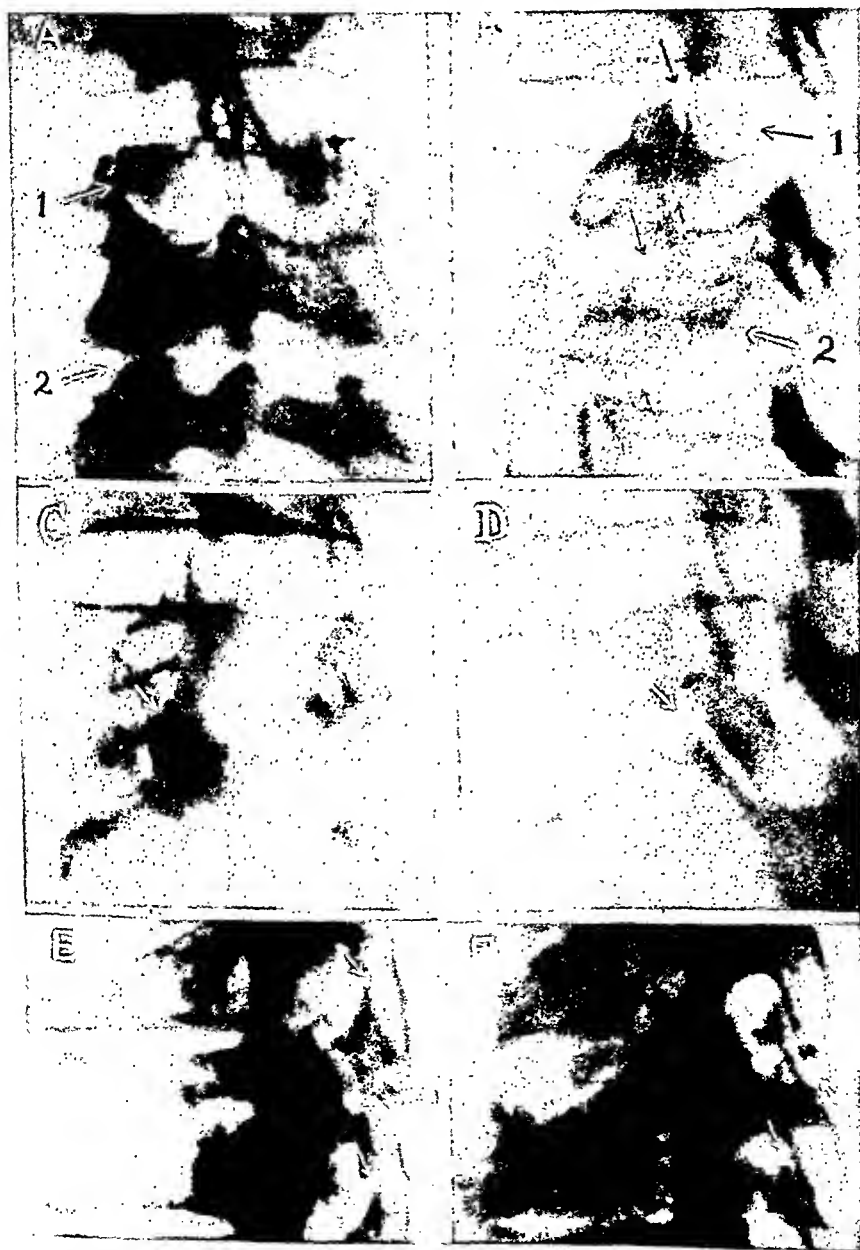


Fig. 2.—Sources of errors. In the sagittal view (A) two facets appear to be ragged and their joint spaces narrowed (arrows); but the oblique view (B) shows that they are normal. Owing to faulty positioning (C and E) the joint spaces appear ankylosed, but correct projections (D and F) show normal joints (arrows).

joint may be present between the first and second sacral vertebrae, especially when their transverse processes are not completely fused (lumbarization) (Fig. 3).



Fig. 3.—Developmental variations. Cervical spine of a newborn (A) with normal gaps between bodies and arches. In a boy, aged 12 years (B), the articular processes are broad and short. In a woman, aged 20 years (C), there is a synostosis between the second and third cervical articular processes. In a young man (D) the articular processes of the same vertebra differ in size, shape, and position. Hypoplasia (E) and aplasia (F) of inferior articular processes. Supernumerary joint (G) between first and second sacral vertebrae.

ARTHRITIS

The roentgenologic interpretation of arthritis is not built on firm ground. Apart from technical limitations, difficulties and confusion

arise from the combining and overlapping of morbid processes that are usually believed to be distinctive. For instance, bone atrophy, considered as typical of atrophic (rheumatoid) arthritis, occurs in both main types of arthritis;¹² whereas, condensation and osteophytes, which are regarded as criteria of hypertrophic (osteo-) arthritis, may develop also in the atrophic form when the articular bone has sufficient vitality to react by hypertrophy to the stimulation which results from the loss of cartilage.¹² Severe inflammation, irrespective of its etiology, is always

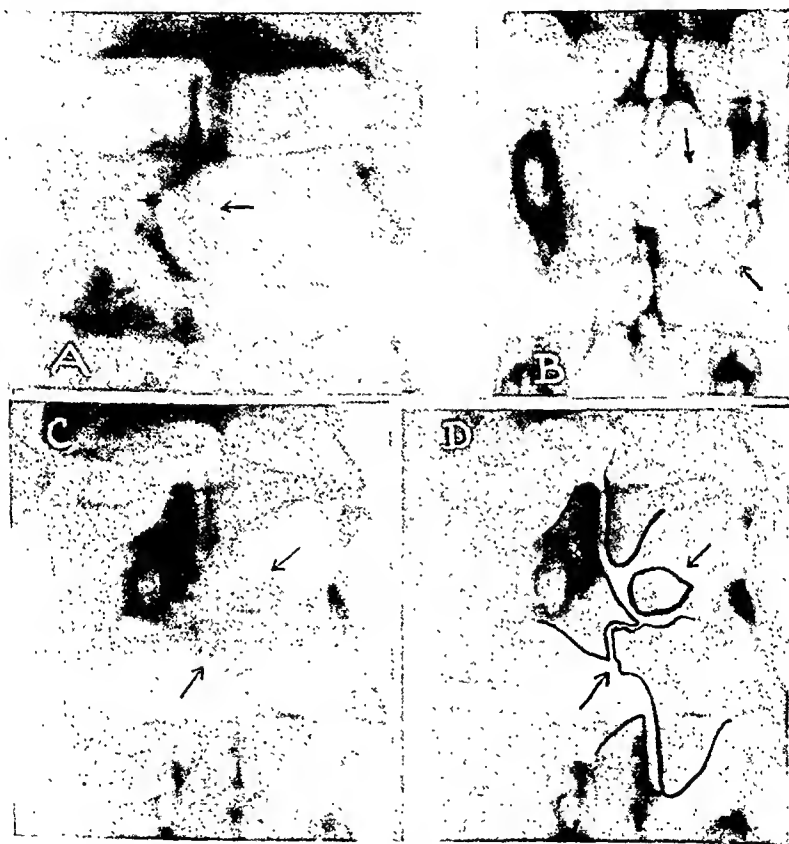


Fig. 4.—Gap in tip of articular process of lumbar vertebra (A). Sagittal view (B) and oblique views (C and D), showing gap in isthmus and a supernumerary ossicle close to it.

associated with rarefaction;¹⁵ all being equal, a weak or oft-repeated stimulus elicits hypertrophy.²² Infectious, toxie, metabolic, and mechanical influences are often intertwined. An infectious arthritis may be reactivated by mechanical or endocrine factors, and lesions caused by mechanical damage to cartilage are often aggravated by toxic or infectious influences. The alternation of inflammation and repair leads then to appearances difficult to analyze.

Bearing in mind that we are thus dealing with variable reactions to variable stimuli rather than with defined entities, we may follow the accepted distinction between an atrophic (rheumatoid) and a hypertrophic (osteo-) arthritic type, but without assigning to either a specific cause.

Atrophic (Rheumatoid) Arthritis.—One of its first stages is enlargement of the joint capsule. This is occasionally visible in the cervical segments, where the intervening soft tissues are thin enough to permit of visualization of the shadow cast (Fig. 5). Such a swelling of the joint capsule may occur also in joints involved by hypertrophic arthritis (Fig. 6 C). Slight rarefaction of the articular processes, stippled or diffuse, may coexist with the swelling in atrophic arthritis.¹⁷ Atrophic arthritis may heal at this stage, and the shadow then disappears. If it progresses, the articular cartilage thins down, whereby the visible joint space becomes narrow (Fig. 5). Effusion, which often counterbalances this narrowing in other joints, seems to be very rare in the apophyseal articulations. Once destroyed, the cartilage is not regenerated to any appreciable amount or degree. The inflammatory pannus and cellular infiltration erode the subcartilaginous bone, and the facets become scalloped or ragged (Fig. 5). The disease may become arrested at this stage, at least for indefinite periods.¹⁷ One of two reactions may set in subsequently. Either the denuded bone becomes condensed and rough (Fig. 5 F), whereby the atrophic merges with the hypertrophic form; or the inflammation may recur or progress and bony ankylosis between the facets take place (Fig. 5 C, F). Sometimes both forms of reaction are observed in the same vertebral column (Fig. 5 F). When bony ankylosis occurs, the ligamenta flava usually ossify together with the joint to which they adhere.

The lesion in its different phases may be confined to one or a few of the apophyseal joints;¹⁷ it may also involve gradually those of the entire spinal column. The latter condition is invariably associated with all the clinical symptoms of rhizomelic spondylosis (Strümpell-Marie disease, ankylopoietic spondylitis or spondylarthritis, the Bechterew disease of the German nomenclature).

The roentgenologic study of rhizomelic spondylosis confirms the experience that autoptic findings are often misleading. "One does not die of rhizomelic spondylosis,"¹⁴ hence post-mortem examination shows only the final result of this malady. Ossification of the longitudinal and yellow ligaments being common at advanced stages, the disease has been regarded as a form of spondylitis ossificans ligamentosa. Fagge's famous specimen, shown in Knaggs' article,¹² does not present ossification of the longitudinal ligaments. Léri, whose description is still unsurpassed, took great care to point out that ossification of vertebral ligaments occurs in many other lesions of the spine.¹¹ My studies suggest that vertebral ligaments may calcify or ossify in sections whose mobil-

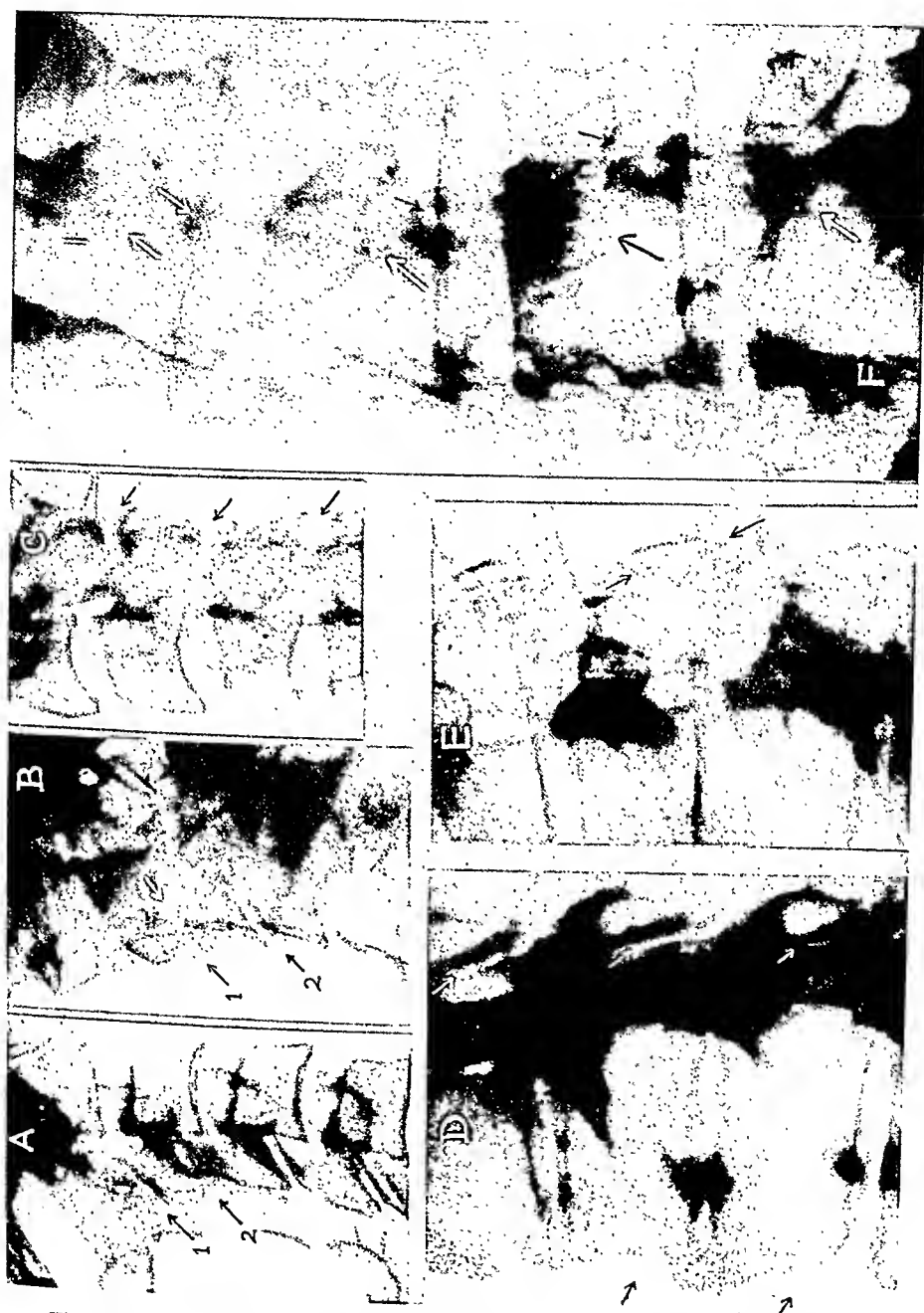


Fig. 5.—Atrophic (rheumatoid) arthritis. Lateral (A) and oblique (B) views, showing at Arrow 1 a narrowed joint space with ragged facets. Compare with the normal of apophyseal joints in the absence of ossification of ligaments; complete rigidity. Compare with D, dorsal spine of another case, showing ossification of anterior longitudinal ligament in the absence of lesions of apophyseal joints; no clinical symptoms whatever. Ankylosis confined to one dorsal joint (E). Rhizomelic spondylosis (F); condensed facets, showing that hypertrophic reactions may occur in the course of an atrophic arthritis.

ity is diminished for any of various reasons.¹⁷ Where the disks are thinned, the longitudinal ligaments become flabby and tortuous, their ossification taking place in the form of protruding spicula. Where the disks remain normal in height, as in rhizomelic spondylosis, the ligaments remain stretched and ossify accordingly. This bamboo spine is one of the results, but it is neither a primary lesion nor a constant element of the morbid process; the longitudinal ligaments may fail to ossify in patients in whom complete ankylosis is unmistakable; in these, however, the apophyseal joints are invariably involved (Fig. 5 C). On the other hand, when the ligaments are ossified in the absence of apophyseal arthritis, clinical symptoms are not usually present (Fig. 5 D).

The vertebral bodies are often rarefied in rhizomelic spondylosis. Serial radiographs have shown that rarefaction is most severe while the arthritic inflammation is active; the vertebral bodies regain normal bone density when ankylosis between the facets has taken place.¹⁷ We may assume that the vertebrae rarefy in this case like any other bone adjacent to an inflamed joint. Vertebral rarefaction and ossification of ligaments are perhaps interdependent. Connective tissue does not usually ossify unless neighboring bone is rarefied simultaneously.¹⁸ This is a modern version of Marie and Léri's view that ossification of vertebral ligaments is a mode of healing, a reparative strengthening of the weakened spine, and merely an example of a general biologic rule.¹⁴

Hypertrophic (Osteo-) Arthritis.—As in other joints, its incipient stages cannot often be recognized radiographically in the apophyseal articulations. In the absence of definite bone rarefaction, narrowing of the joint space due to thinning of cartilage may suggest this lesion before bone hypertrophy develops. But, as above mentioned, such a finding may correspond also to a quiescent or arrested atrophic arthritis; the two forms may then be indistinguishable even histologically.¹²

When more advanced, hypertrophic arthritis is revealed by well-marked condensation of the articular processes. The joint space is narrowed. Osteophytes form at the edges of the facets. Contiguous exostoses may fuse and produce ankylosis of the joint (Fig. 6). Thorn-shaped prominences at the tips of the articular processes correspond to ossified insertions of intra-articular ligaments. This may be associated with hypertrophic spondylarthritis,¹³ but it may also occur independently.¹⁷ The two conditions should not be considered identical.

Hypertrophic spondylarthritis is not uncommon in the dorsal spine, where it often occurs in the absence of other vertebral lesions. In the lumbar section hypertrophic arthritis of the apophyseal joints is often associated with thinning of intervertebral disks. As the distance between vertebrae at the level of a flattened disk diminishes, the cartilages of the facets sustain increasing stress. Where the plane of the facets slopes diagonally backward, a posterior shift of the superjacent vertebra

results from thinning of the disk (Fig. 6). The subluxation may amount to bony impingement of the articular process upon the adjacent vertebra,⁹ but the apophyseal cartilage may resist the strain.¹⁷ This accounts for the fact that at the level of a flattened disk the apophyseal joints may remain normal; whereas, the corresponding vertebral bodies

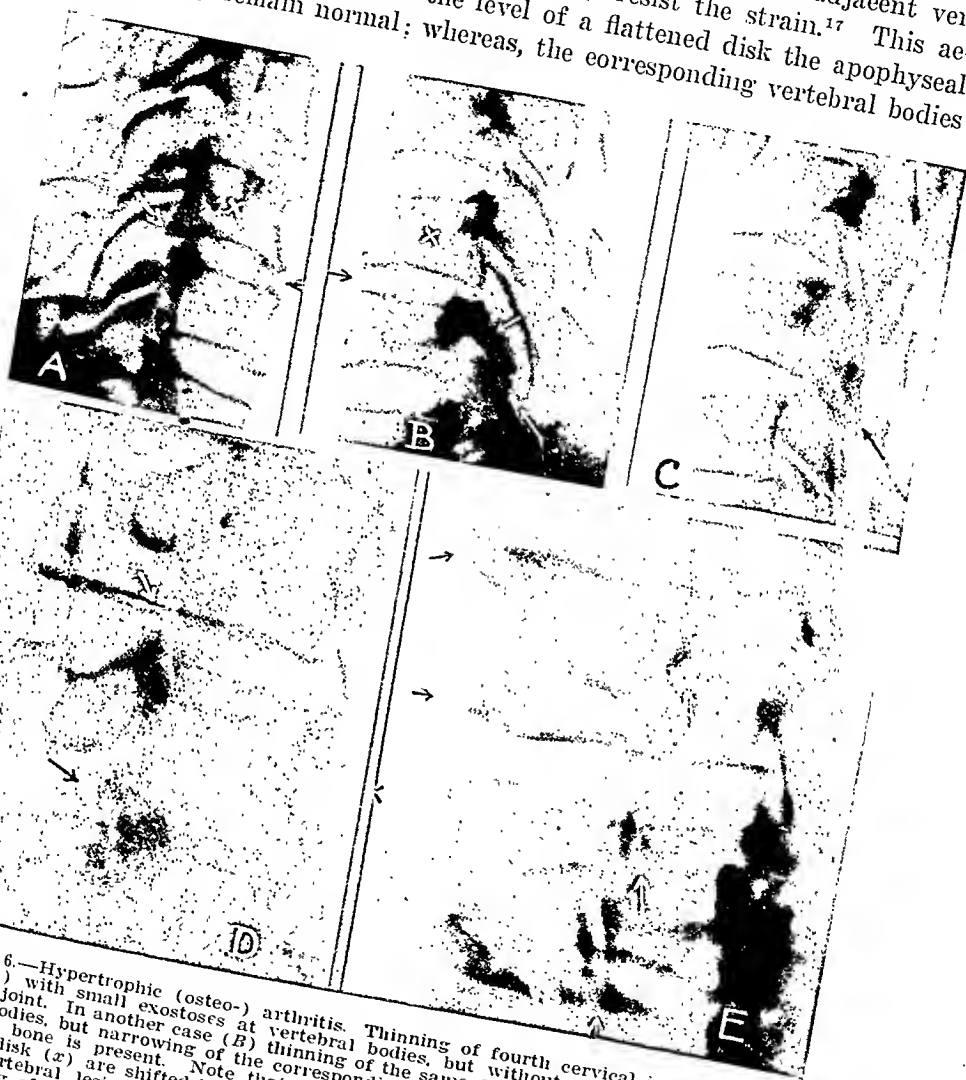


Fig. 6.—Hypertrophic (osteo-) arthritis. Thinning of fourth cervical intervertebral disk (A) with small exostoses at vertebral bodies, but without changes in the apophyseal joint. In another case (B) thinning of the same disk has not induced exostoses at the bodies, but narrowing of the corresponding joint space and condensation of the articular bone is present. Note that in either case the vertebral bodies above the thinned disk (x) are shifted backward. Hypertrophic arthritis (C) in the absence of other vertebral lesions. Note the shadow of the swollen joint capsule (arrow). Flattening of lumbar intervertebral disks: hypertrophic arthritis of apophyseal joints (D) in the absence of vertebral osteophytes; in another case there are large vertebral osteophytes (E), but the apophyseal joints are normal.

show large exostoses. In other cases the apophyseal cartilage is damaged while the vertebral bone fails to respond by hypertrophy to the mechanical irritation caused by disk flattening (Figs. 6, 8). In the first case it is the bone which reacts; in the second, it is the cartilage which is injured. These are clearly different reactions, but, since both are

often regarded as corresponding to the same lesion, namely, osteoarthritis of the spine, their failure to be always associated with disk thinning and with each other has given rise to extensive discussions and many discrepancies. I have suggested that lesions consecutive upon thinning of disks be designated as diseogenetic in order to distinguish

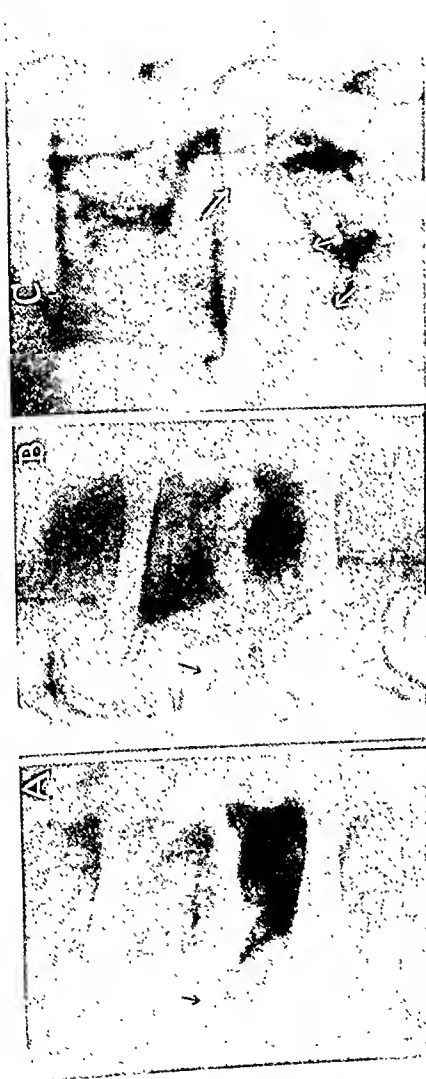


Fig. 7.—Pott's disease; nineteen months' interval between A and B. Neural arches and articular processes remained normal. In another case (C) rounded areas of rarefaction are seen in the articular process six months after onset of symptoms.

them from other forms; yet the diseogenetic type of apophyseal arthritis and that of vertebral osteophytes are distinct in spite of their common etiology. The first, hypertrophic,¹⁷ deforming,¹⁸ or marginal²¹ spondylitis, is essentially an osteitis related to callus formation; the second, hypertrophic spondylarthritis, corresponds to the hypertrophic arthritis of other joints. They may coexist, but they differ in nature. Any mechanical strain may affect either the vertebral bodies or the

apophyseal cartilage,¹³ or both. This depends on the type of traumatism as well as on the vulnerability and the ability to react of the different tissues.

Clinical findings suggest that osteoarthritis in the apophyseal joints may be caused by chronic infection with *Endamoeba histolytica*,¹⁷ but experimental or histologic proof is not yet available.

SECONDARY INVOLVEMENT

Infection may spread from the vertebral body into the articular process and thus involve the apophyseal joint.^{13, 17} This is rare since the compact bone of the arches and their processes is less easily invaded than the cancellous vertebral body. For instance, in vertebral tuberculosis the articular processes usually remain intact even when the disease persists for many years (Fig. 7). On the other hand, primary tuberculosis of cervical apophyseal joints may spread into the bone.¹² The joints may become involved when osteomyelitis localizes in the neural arch.²³ Primary osteomyelitis of articular processes without involvement of other parts of the neural arch was reported very recently.²⁰

TRAUMA

Fractures of the articular processes may be combined with fractures or compression of the vertebral bodies,¹ but they are rare as independent injuries.^{1, 17} Supernumerary ossicles, separated by cartilage from the main part of the articular process, may be dislodged by trauma.^{1, 16, 17} Gaps in the isthmus may be widened by postural and traumatic factors, which is well known to result in spondylolisthesis.² The subjacent apophyseal joint may then be exposed to increased static stress¹³ and will respond to it by hypertrophic arthritis. Any other abnormal position of vertebrae may lead to similar reactions.

CLINICAL RELATIONS

Since the vertebral column is composed of many bones with numerous interacting joints, none of which is easily accessible to inspection and palpation, the clinical diagnosis of vertebral disease is based on combinations of uncharacteristic findings: pain, local and radiating; diminished mobility; and abnormal posture. Except in the cervical section, the apophyseal joints are covered by thick layers of muscles and cutis; their inflammation cannot be recognized by the presence of swelling or redness; the pain it elicits is difficult to localize; and diminished mobility, if it becomes evident at all, may be accounted for by lesions of other vertebral parts. Radicular pain may be caused by any morbid process that encroaches upon the neural foramen. Thus, we cannot expect to find pathognomonic signs and symptoms.

Like arthritis of other joints, apophyseal arthritis (spondylarthritis) is associated with local pain during active phases.^{12, 14, 17} When the inflammation is arrested, or when bony ankylosis prevents further irrita-

tion, local pain usually subsides. This is quite evident in rhizomelic spondylosis. The pain is due, at least in part, to muscle tension over the involved joint. When numerous apophyseal joints are affected, a large section of the back shows this muscular guarding and the back is then held stiff constantly, even during rest at night. This is probably responsible for the fact that ankylosis takes place later in the position of extension, such as in poker back. No other direct influence of spondylarthritis upon the position of the spine can be found. Pressure upon nerve roots may be caused by swollen joint capsules, by exostoses



Fig. 8 A and B.—Mobility of cervical spine in two cases with thinning of fourth and fifth intervertebral disks. Extreme flexion and extension. In the first patient (A and B) the apophyseal joint spaces at the level of the flattened disk are narrow and the facets are irregularly bounded (discogenetic spondylarthritis); the segments involved are almost immovable.

at the articular processes, or by calcification of periarticular tissues;¹⁷ wherefore signs and symptoms of radicular neuritis may occur at various stages of the arthritic process and persist after the inflammation has subsided.

The question of normal and pathologic mobility of the column cannot be discussed here, being so involved as to necessitate a separate report.²⁵ It may be stated that mobility is almost invariably diminished in sections which contain a diseased apophyseal joint; whereas, many other

vertebral lesions may and do fail to impair vertebral movements. For example, in segments with thinned disks flexibility usually remains normal as long as the apophyseal joints at this level are not affected (Fig. 8).

Backache, stiffness, and radicular pain are caused by certain lesions of the spine more frequently than has been appreciated in the past; this, however, has perhaps been overemphasized in recent reports, not excluding my own. It has to be borne in mind that extensive lesions of the vertebral column may fail to cause any clinical manifestations.¹⁷ Certainly pain in the back and limbs may occur, recur, or persist in the absence of any vertebral anomaly; yet growing experience seems to show

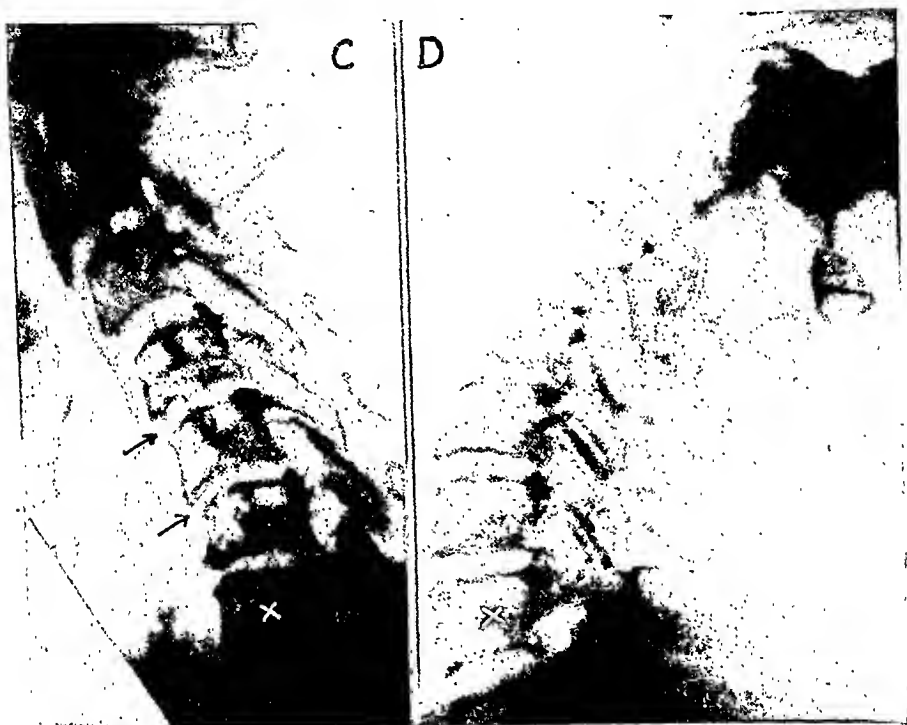


Fig. 8 *C* and *D*.—In the second patient (*C* and *D*) the apophyseal joints are not involved, and mobility is normal in spite of the thinned disks. The pictures are so taken and reproduced that the vertebra marked by *x* keeps the same position during the movements.

that, when clinical symptoms coexist with a demonstrable vertebral lesion, the nature and severity of the clinical manifestations depend to an appreciable degree upon the involvement of the apophyseal joints.¹⁷ Local pain or tenderness of a vertebral segment, associated with rigidity of the section involved, usually means that one or several of the apophyseal joints at this level are involved either primarily or secondarily.

CONCLUSIONS

The apophyseal joints may be involved by the various forms, phases, and combinations of arthritis in the same manner as the small joints of

the hand or foot. The roentgenologic and clinical findings are those of arthritis. Atrophic (rheumatoid) arthritis is always a primary lesion; hypertrophic (osteo-) arthritis may be associated with, or induced by, other vertebral anomalies, especially thinning of intervertebral disks. Both forms are distinct from the so-called arthritis of the spine which consists essentially in exostoses at the edges of the vertebral bodies. The conception of arthritis, pertaining to lesions of diarthrodial joints, does not apply to the disk synchondrosis either anatomically or clinically; the reactions at the edges of the vertebral bodies are osteitic, but not arthritic. It is in the apophyseal joints that arthritis of the spine, or spondylarthritis, is localized. The clinical signs and symptoms are discussed briefly.

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Editorials

Nutritional Disturbances in Surgical Practice

UNTIL relatively recent times many surgeons regarded metabolic and nutritional disturbances as matters far removed from their province and of limited practical significance in the management of surgical disorders. The changing trend of the times is apparent in the character of numerous articles which have appeared in this and other journals; it is now generally known that a number of common abdominal ailments are not infrequently attended by deficiency states which have a profound influence on the course of the disease and upon the surgical risk. The occasional development of pellagra in cases of long-standing pyloric obstruction and the relatively frequent occurrence of hypoproteinemia and nutritional edema in cases of disturbances in the continuity of the gastrointestinal tract may be cited as illustrative of this fact.

Disease processes affecting the small intestine offer even more of a hazard in this respect; here multiple deficiency symptoms are, as a rule, apparent and the nutritional disorders may, in fact, overshadow the primary disease. The elimination of the absorptive function of considerable portions of the small intestine by inflammatory lesions, by resection, or by short-circuiting operations of various types is capable of producing every grade and type of avitaminosis and nutritional disorder. Mackie and Eddy¹ have recently published a report of a patient with regional ileitis who at various times gave evidence of scurvy, tetany, peripheral neuritis, and hypoprote thrombinemia, the latter being due to vitamin K deficiency; in this individual the concentrations of carotene and vitamin A in the blood were also greatly reduced. In this same connection one recalls the curious macrocytic hyperchromic type of anemia associated with intestinal strictures which may well be due to failure of the absorption of the antiper-nicious anemia principles. Patients suffering from chronic intestinal disorders or even from chronic pancreatic insufficiency with steatorrhea may suffer from the more or less complete clinical syndrome of sprue, long noted for the number and variety of metabolic disturbances associated with it. The fundamental defect in each instance is, of course, failure of normal absorption in the small intestine.

For exactly the same reason, gastrojejunoocolic fistulas may also be responsible for a variety of deficiency syndromes, especially if they are of large caliber and of long duration. In one selected group of twelve

such cases in which the patients died after operation, nutritional edema was encountered seven times; tetany, glossitis, and pellagra each three times; and a hemorrhagic diathesis, caused by failure of absorption of vitamin K, four times.² Fatty metamorphosis of the liver was a feature in eight of these cases, a fact which is of particular interest when one recalls the rather constant finding of a fatty liver in cases of fatal pellagra. Whether the changes in the liver are due to deficiencies in the absorption of choline and its derivatives, or whether defective utilization of nicotinic acid may play a role cannot be stated with certainty. The added surgical risk imposed by a hepatic lesion of this type and by the actual or latent prothrombin deficiency need not be emphasized. The cases cited above, of course, are extreme examples, but they do indicate the necessity of considering actual or potential nutritional disturbances in the treatment of patients with intestinal lesions.

The so-called subclinical vitamin deficiencies which may be present in certain affections of the abdomen requiring surgical treatment are not sufficiently well recognized to warrant detailed consideration at present, although they are doubtless of clinical importance. It may be said, however, that many individuals, because of long illness and a limited diet, are dangerously close to a "deficiency level" in respect to one or more vitamins. The added insult of an anesthetic and a surgical procedure, and the further reduction in food taken during the postoperative period, may precipitate a dangerous avitaminosis. This is particularly likely in respect to the "coagulations vitamin" which is stored only in small quantities and for which a critical level of deficiency is so easily attained. It is less true of the antineuritic vitamin, the body stores of which may be exhausted only after somewhat longer period of time.

Without succumbing to the importunities of those who have vitamin products to sell or without becoming unduly conscious of minor variations in the concentration of certain vitamins in the blood and urine, the surgeon can do much to advance the knowledge of deficiency states and at the same time do his patient a great service by keeping watch for the early signs of nutritional disturbances and treating them adequately. They may not be encountered frequently, but even their rare occurrence is of the greatest surgical significance.

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—Albert M. Snell, M.D.

Rochester, Minn.

Suction Drainage in the Management of Intestinal Obstruction

THE REMOVAL of material by means of suction from the gastrointestinal tract in acute intestinal obstruction has become so widespread in its application that it is frequently referred to as a form of treatment for this condition, rather than as a method for decompression of distended intestine. To those responsible for the introduction and popularization of suction drainage, the procedure has been considered a means of effecting decompression of the bowel and not specifically a method of treatment of intestinal obstruction. Wangensteen and his associates have clearly stated the limitations as well as the advantages of suction drainage applied to the therapy of intestinal obstruction and have emphasized the importance of control of distention in treatment. That it has occasionally been misapplied or badly handled by those lacking an understanding of the general problems involved, the details incident to, or the patience necessary for the application of the procedure is no fault of the procedure nor of those who have found it indispensable in the treatment of intestinal obstruction.

Distention, long recognized as a dominant diagnostic feature of uncomplicated intestinal obstruction, has not received adequate consideration as the main factor responsible for lethal pathologic changes in the patient. Much interest has been displayed concerning toxemia, dehydration, and shock as causes of death, but there has been a tendency to consider lightly the role of distention in initiating these grave phenomena. Within the past ten years there has been adequate proof from clinical as well as laboratory observations to indicate that, even in the presence of complete obstruction, toxemia or shock does not occur if distention is controlled and strangulation is not a factor. Any attempt to differentiate between operative and nonoperative methods of treating intestinal obstruction indicates a lack of understanding of the general problem. Intestinal obstruction is not a single clinical entity but a variety of problems associated under one heading because of common features; i.e., the inability of the intestine to propel its contents untrammelled throughout its entire length and the early development of distention.

The lack of appreciation of the importance of the control of distention in intestinal obstruction has contributed to the high mortality of this condition. Removal of intestinal content by suction drainage is but a simple and efficient means of overcoming one very basic factor in intestinal obstruction. The level at which suction is exerted depends on the needs of the patient. The majority of cases may be decompressed by means of a catheter placed into the duodenum. The nearer the obstruction suction is exerted, the more efficient decompression is likely to be. Suction exerted just above the obstructed area decompresses the bowel as efficiently as enterostomy performed at the same point and has the same advantage with regard to feeding the patient. The mortality and

morbidity ascribable to intestinal intubation is decidedly less than in the case of enterostomy, and the method is more certain of accomplishing results.

Treves (1884) condemned the use of enterostomy on the basis that it did not relieve the obstruction. More modern writers have expressed the same viewpoint, but it ought to be emphasized that enterostomy, like suction drainage, is but a means of relieving distention. In adynamic ileus enterostomy is more likely to increase the ileus than diminish it. Enterostomy for small bowel distention has become a rare procedure, due chiefly to the realization that distention may be controlled as well by suction drainage and with less danger to the patient.

Control of distention is but one phase of the management of intestinal obstruction. The control of dehydration by the administration of fluids and salt is not considered a method of treatment in intestinal obstruction, yet it is quite an essential part of the problem of therapy, as is blood transfusion. Removal of an obstructing lesion is of major importance but should be done after the patient has been prepared for operation. Suction drainage applied to whatever level of the intestinal tract necessary to accomplish results is the most dependable and safest procedure available for the control of distention. The fact that in many cases adequate decompression suffices to relieve the obstruction does not alter the fact that actually suction drainage is but a means of controlling distention. As such it plays an indispensable part in the program of management of intestinal obstruction.

—Charles G. Johnston, M.D.
Detroit, Mich.

The Clinical Relationship of Pancreatic Disease to Fatty Infiltration of the Liver

THE ESTABLISHMENT of fatty infiltration of the liver and pancreatic disease (fibrosis and necrosis) as a clinical entity is another of the innumerable examples of successful application of experimental data to the better understanding of disease in the human being. For the most part, the recognition of the disease in the human being was dependent upon the experiments of Fisher¹ and Allan and associates² (1924), who demonstrated that pancreatectomy in dogs led to death of the animal in two to eight months with fatty infiltration of the liver, in spite of the administration of insulin, but that death and fatty infiltration of the liver could be prevented by feeding raw pancreas. Hershey and associates³ noted that the animals could also be saved by feeding lecithin and choline. One of the most important contributions made to the subject was the discovery by Dragstedt and associates⁴ that an alcoholic extract of pancreas, named lipocain by them, would prevent or cure fatty infiltration of the liver induced by pancreatectomy.

Pathologists are aware of the fact that fatty infiltration of the liver (without concomitant pancreatic disease) is a very common lesion, but that the exact mechanism of its development is unknown, except in the instance of the lesion herein discussed, which is a rather uncommon disease. In general, it is agreed that fat is deposited in the liver subsequent to certain types of hepatic damage. However, in the pancreatic-hepatic syndrome under discussion we have no evidence of the production of hepatitis by the pancreatic disease; it would appear more reasonable to explain the fatty deposit in the liver in this instance on the assumption that in certain types of pancreatic disease an important substance (named lipocaine by Dragstedt) which is necessary in fat metabolism is no longer produced by the pancreas.

Much credit is due Snell and Comfort⁵ for establishing the importance of the pancreatic disease to the fatty infiltration of the liver in adults. In analyzing six cases reported in the literature and one I encountered, it is apparent that numerous types of processes may be the primary lesion responsible for the pancreatic damage. In two of the three cases reported by Snell and Comfort, pancreatic lithiasis appears to have been the major etiological factor. In the case I encountered, gall bladder disease (cholelithiasis) appears to have been the initial lesion, producing a pancreatitis, which in turn gave rise to the fatty change in the liver. Gall bladder disease is present in two or three of the other cases available for study, but it is difficult to determine whether this was the direct cause of the pancreatic lesion. It is well known that gall bladder disease is present in 80 to 90 per cent of patients with acute pancreatitis. Even though it is obvious that fatty infiltration of the liver is not commonly associated with this type of pancreatitis, it is my opinion that, after a large series of patients with pancreatic-hepatic disease are studied, gall bladder disease will stand out as one of the most important etiological factors in adults. The mere fact that fatty infiltration of the liver is rarely encountered in the acute edematous and hemorrhagic types of pancreatitis does not eliminate these well-known types of pancreatitis from the pathogenesis in the pancreatic-hepatic syndrome, since it takes weeks or months for the fatty infiltration in the liver to develop.

The manifestations of the so-called pancreatic-hepatic syndrome are dramatic, although a few are insidious and obscure. Weakness and malaise are perhaps the earliest symptoms; mild epigastric pain and distention are common. Nausea and vomiting may be complained of. Steatorrhea is usually present but not always. Absence of pancreatic enzymes in the duodenal secretions is very helpful in establishing the diagnosis, but probably not a necessary finding. At least in the advanced cases, one of the most constant findings will be enlargement of the liver, incident to the fatty infiltration in the liver. Diabetes of a peculiar type may be present. With the information available at the present time, it

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

LOBECTOMY FOR BRONCHIECTASIS

BRIAN BLADES, M.D., ST. LOUIS, MO.

*(From the Chest Service of Barnes Hospital and the Department of Surgery,
Washington University School of Medicine)*

THE extirpation of the diseased portion of the lung as a treatment for bronchiectasis was considered as early as 1881, when Gluck¹ and others performed animal experimentations with lobectomy. In 1901 Heidenhain² was credited with a successful case in man. A quarter of a century later, however, the feasibility of radical surgery for bronchiectasis was still in doubt, both because of high operative mortality and the failure to achieve entirely satisfactory clinical results in surviving patients.

In 1932, Graham, Singer, and Ballou³ collected data concerning 212 cases of bronchiectasis treated by lobectomy. The operative mortality for the entire group was 34 per cent and only 47 per cent of the survivors attained complete symptomatic relief. In the larger and more representative series the operative mortality approached 50 per cent. It is understandable why considerable courage was necessary on the part of both the patient and the surgeon when lobectomy was undertaken a few years ago.

The almost incredible improvements in the surgical treatment of bronchiectasis which have occurred in the past decade are best illustrated by including samples of recent statistics on lobectomy reported by various surgeons throughout the world. It is noteworthy that Sauerbruch, Graham, and Churchill's cases are included in the statistics collected in 1932 and it is now possible to cite the results of the same surgeons eight years later.

In England Edwards⁴ has reported 166 cases of lobectomy with a mortality rate of 12 per cent. Only 2 deaths occurred in his last 54 cases. Sauerbruch,⁵ of Germany, reports a 12 per cent mortality in 58 cases. At the Norwegian State Hospital, Oslo, Holst⁶ has performed 12 lobectomies with 1 death. This fatality occurred in a case of bilateral bronchiectasis. The patient survived the first lobectomy, but died after the operation on the other side. In this country Churchill⁷ has reported 84 cases with a mortality rate of 4.7 per cent. Sixty-six instances of unilateral lobectomy with only 1 death are included in his group. Graham,⁸ O'Brien,⁹ Lindskog,¹⁰ and others have reported series of cases with mortality rates of approximately 5 per cent. It is safe to conclude, therefore, that in competent hands an operative mortality

appears that pancreatic disease (fibrosis and necrosis) is a prerequisite. Rosenberg⁶ and Snell and Comfort⁵ have demonstrated the efficacy of lipocaic in treating the disease.

Fatty infiltration of the liver associated with pancreatic disease of a fibrotic type is well known to pediatricians and quite common; it is known as congenital pancreatic steatorrhea. In this group of cases congenital anomalies, such as absence or atresia of pancreatic ducts, appear to be the most important of the etiological factors. So far as could be determined by my perusal of the literature, no one has suggested that this disease and the fatty liver secondary to pancreatic disease in adults are related. However, the clinical manifestations are identical; the only difference of significance appears to lie in the etiological factors. Although pancreatic lithiasis and gall bladder disease are the most obvious factors in the production of the pancreatic disease in adults, it is very likely that congenital anomalies, such as stenosis of ducts, may finally result in the production of enough pancreatic damage to give rise to the disease later in life. For these reasons it appears justifiable to conclude that congenital pancreatic steatorrhea and the pancreatic-hepatic syndrome (fatty infiltration of the liver and pancreatic fibrosis) of adults are the same disease. Because of growth demands made by the child's body, there may be more nutritional dysfunction including vitamin deficiency in the disease in childhood; however, the major points of difference are the etiological factor and the age of the patient.

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—Warren H. Cole, M.D.

Chicago, Ill.

disease, it was not until twenty-seven years later that Sicard and Forestier¹⁶ introduced lipiodol and furnished an accurate method for localizing bronchiectasis in the living patient.

As many of the improvements in the results of lobectomy are attributable to expert interpretation of lipiodol bronchograms and a better understanding of the surgical anatomy of the tracheobronchial tree, it is important to direct attention to certain facts concerning the localization of bronchiectasis which in the past have not been appreciated.

The conception that bronchiectasis is primarily a disease of the lower lobes is undoubtedly responsible for many unsatisfactory results of lobectomies for bronchiectasis. The common combination of involvement of the lingular division of the left upper lobe and the right middle lobe in association with bronchiectasis of the corresponding lower lobe has been emphasized recently by several authors. In 49 cases subjected to lower lobe lobectomy by Churchill,¹⁷ 33 per cent of the patients had involvement of either the lingula of the left upper lobe or of the right middle lobe. O'Brien⁹ cites 11 cases of unilateral bronchiectasis, 4 of which showed bronchial dilatations in the left lingular bronchial division or in the right middle lobe. In 47 cases of lower lobe bronchiectasis studied by Myers and Blades,¹⁸ 57 per cent of the patients with left lower lobe bronchiectasis also had involvement of the lingula of the left upper lobe. Right middle lobe bronchiectasis was present in 59 per cent of the patients who had diseased right lower lobes. The combination of left lower lobe bronchiectasis and bronchiectasis of the lingula of the left upper lobe is so frequent that Churchill and Belsey¹⁹ consider segmental pneumonectomy a more appropriate descriptive term than lobectomy when left-sided lesions are encountered. In their excellent article they describe the surgical anatomy of the lingula of the left upper lobe and further emphasize the frequency of bilobar involvement. Sauerbruch²⁰ had noted this frequent distribution of bronchiectasis in a study of autopsy specimens before lipiodol bronchograms were available. Unfortunately, his observations did not receive the attention they deserved. Neither technical difficulties nor operative risks are increased by removing the lingula of the left upper lobe or the right middle lobe when the corresponding lower lobe is resected. Failure to excise all of the diseased tissue, of course, will result in unsatisfactory clinical results.

Various methods have been suggested for the administration of lipiodol, but it is of no great importance which technique is employed so long as each segment of the lung is visualized and the bronchograms are interpreted properly. Goldman and Adams²¹ recently reported a method of endobronchial probing through a bronchoscope by which each bronchial segment may be visualized separately. The introduction of the oil by tracheal puncture or by means of a nasal catheter has been advocated also. We are of the opinion, however, that the ad-

of less than 10 per cent may be anticipated in uncomplicated cases of bronchiectasis subjected to lobectomy. It is equally important to record that in the great majority of the reported cases clinical cures have been accomplished by the operation.

That the increasingly successful application of surgical therapy is not solely attributable to technical advances becomes apparent when it is realized that, in spite of the uniformly good results from modern lobectomy, operative technique is far from standardized at the present time. It is desirable, therefore, to enumerate certain other factors which have made the present respectable status of the operation possible.

APPLICATION OF FUNDAMENTAL PHYSIOLOGIC PRINCIPLES

The hazards of opening the free pleura were appreciated by the pioneers of thoracic surgery and for many years constituted the greatest obstacle to intrathoracic operations. In 1904, Sauerbruch¹¹ introduced the negative pressure chamber. This was later modified by Meyer¹² in the form of a positive pressure chamber within the negative pressure chamber which could be used when necessary. The principles of these inventions to prevent the dangers of open pneumothorax were sound, but their practical application was clumsy and difficult.

Meltzer and Auer¹³ in 1909 introduced intratracheal anesthesia. Its use, however, was limited and it was not until surgical opportunities of World War I necessitated extensive thoracic operations that intratracheal anesthesia was widely employed. During this same period, certain emergencies stimulated research in the physiology of the chest which resulted in the establishment of basic principles which influenced the whole future of thoracic surgery. Among the most important of these, from the surgical standpoint, was the work of Graham and Bell¹⁴ on the effect of altered intrapleural pressures in intrathoracic operations and the relationships of open pneumothorax and vital capacity. The general appreciation and acceptance of the principles elucidated during this period make an extensive discussion of the physiology of the chest unnecessary. It is important, however, to realize that modern thoracic surgery may be dated properly from the time of the first world war, and its rapid progress has in a large measure been dependent on the fundamental surgical physiology learned at that time. Once the effects of open thoracotomy on the circulation and respiration were understood and an anesthesia technique perfected to control intrapulmonary pressure in a practical way, subsequent progress in thoracic surgery was rapid.

IMPROVEMENTS IN DIAGNOSTIC STUDY OF THE BRONCHIAL TREE

Although Roentgen's¹⁵ discovery of the x-ray in 1895 marks the introduction of the most important refinement in the diagnosis of chest

lobectomy for bronchiectasis, and in our own series we have had 2 cases of bronchiectasis confined to the middle lobe treated successfully by surgical extirpation. Churchill and Belsey¹⁹ have reported disease of the lingular division of the left upper lobe alone for which they have performed lingulectomy. Regardless of the location of the dilated bronchi, either of the two methods for preparing bronchograms which have been illustrated is satisfactory for preoperative localization of bronchial dilatations.



Fig. 2.—Right anterior oblique (left posterior oblique) bronchogram demonstrating bronchiectasis of left lower lobe and lingula of left upper lobe.

JUSTIFICATIONS FOR RECOMMENDING LOBECTOMY

The studies of Findlay and Graham²⁴ in children, and similar observations of Roles and Todd²⁵ in adults, have established the grave prognosis associated with bronchiectasis. Their work indicates that the disease is progressive and eventually is fatal in the great proportion of cases.

ministration of lipiodol by the simple aspiration method described by Singer²² is preferable to the more elaborate and time-consuming techniques.

Lipiodol bronchograms which are prepared in the frontal projection will not furnish satisfactory delineation of the lingular bronchus on the left or the middle lobe on the right. It is necessary, therefore, to combine frontal and lateral projections with independent filling of the bronchi of each lung, made at intervals long enough apart to allow evacuation of the oil from the lung first visualized, or to employ oblique projections of each side. Bronchograms prepared in the

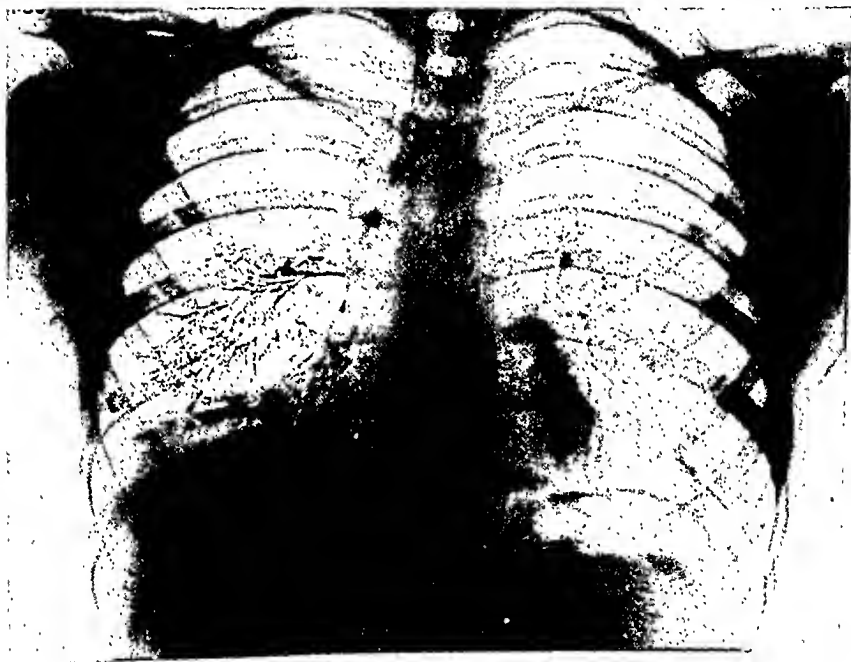


Fig. 1.—Lipiodol bronchogram taken in left anterior oblique projection (right posterior oblique). Note clear delineation of right middle lobe. It was necessary to remove both the lower and middle lobes in this case.

oblique position offer two advantages: (1) Both lungs may be filled at a single sitting without difficulty in distinguishing each bronchial segment and secondary division. (2) Only two x-ray films need to be exposed, as contrasted to twice that number when a combination of frontal and lateral projections are utilized. A bronchogram taken in the right anterior oblique position (left posterior oblique) is employed for the visualization of the left bronchial tree. The left anterior oblique or right posterior oblique is necessary to demonstrate the right bronchial segment (Figs. 1 and 2).

Instances of single lobe involvement other than the lower lobe are not uncommon. Whiteside²³ has reported a successful middle lobe

exceptionally older) with bronchiectasis which is reasonably localized and infected, and in whom there are no serious general contraindications, should be considered as candidates for radical excision of the portion of the lung affected."

PREOPERATIVE PREPARATION FOR LOBECTOMY

The preoperative program is designed to decrease at least temporarily the amount of pus in the bronchiectatic dilatations. The measures employed for this purpose are similar in various thoracic clinics, and it is impossible to know whom to credit for the originality of various details in the preoperative and postoperative management. For convenience, the methods which I have followed at the Barnes Hospital Chest Service in association with E. A. Graham will be described.

The association of chronic nasal sinus disease with bronchorrhea was first noted by Thomson in 1914.³⁰ Practical application of this observation was later suggested by Graham and Singer,³¹ who advocated adequate treatment of infected nasal sinuses in all cases of bronchiectasis and found that there was usually an improvement in the patient's general condition and diminution in the amount of sputum. Therefore, in patients who are considered suitable subjects for lobectomy the first precaution is adequate treatment of infections of this nature.

The second important preliminary to lobectomy is the institution of postural drainage supplemented by bronchoscopic aspirations. The value of bronchoscopy cannot be overemphasized. Not only is diagnostic information concerning possible foreign body, neoplasm, and localization of the lesion essential, but the temporary improvement following bronchoscopic aspiration of pus will often convert the poor risk patient into a reasonably good candidate for a lobectomy. However, when improvement follows a series of bronchoscopic aspirations, it must be remembered that no proved case of bronchiectasis has been cured permanently by this method. Patients should be informed of this fact and made to realize that the risk of lobectomy is proportionate to the amount of active infection in the lungs, and that the optimum time for operation is when symptoms are minimal. The number of bronchoscopic aspirations which will be required depends largely upon the amount of purulent secretion and the patient's general condition.

Compression of the lung by artificial pneumothorax preliminary to lobectomy has been advocated and employed routinely in many clinics. It is doubtful, however, that effectual evacuation of pus-containing bronchi can be accomplished by any form of collapse therapy, and, although the danger is not great, accidental puncture of infected lung during the introduction of air may result in serious complications. The benefits of pneumothorax in causing gradual accommodation to altered intrapleural pressures encountered during the performance of the operation is of doubtful value. It is probable, therefore, that artificial

Even if this were not the case, relief of mental and physical handicaps endured by individuals who regularly cough up foul sputum should justify any procedure which is not accompanied by an excessively high operative mortality. The failure of medical treatment except as palliative, the questionable results obtained with pneumothorax, thoracoplasty, and other forms of collapse therapy in bronchiectasis establish lobectomy as the only completely satisfactory method of treatment. It is, therefore, not so important to define the indications for lobectomy, but rather to know which patients cannot be treated safely by radical surgical intervention.

CONTRAINDICATIONS TO LOBECTOMY

The age of the patient must be considered, and at the present time patients past middle age are not considered suitable risks for lobectomy. The upper age limit will vary in the individual case, depending on the general condition and the extent of the disease. Children tolerate intrathoracic operations particularly well, and for obvious reasons it is desirable to eradicate the disease before irreparable physical and psychological damage is done.

The presence of other serious conditions, particularly cardiovascular disease, of course, will preclude the possibility of lobectomy. The risk of operation is increased if it is attempted in the presence of acute infections of the lung, and, unless serious hemoptysis forces emergency measures, lobectomy should be delayed until the patient is afebrile.

The extent and distribution of the disease must be considered before lobectomy is recommended. Successful trilobe lobectomy has been reported by Overholt.²⁶ Graham²⁷ has removed successfully the right middle, right lower and, eighteen months later, the left lower and lingula of the left upper lobe in a boy 16 years of age. Successful bilateral lobectomies have been reported by Lewis,²⁸ Churchill,²⁹ and others. Total pneumonectomy for unilateral universal bronchiectasis is now so common that it requires no particular comment. It would seem, therefore, that the amount of lung tissue which may be extirpated safely must be determined by a consideration of vital capacity, the patient's age, and other individual factors. In several of my own cases of bilateral bronchiectasis removal of the bronchiectatic portion of lung on one side has been followed by so much improvement that the patients have decided to postpone operation on the other lung. In every instance the more severely diseased lung was operated upon first. Whether these patients will continue to be free of symptoms cannot be determined until more time has elapsed. Our experiences suggest, however, that, even in the presence of extensive bilateral disease, extirpation of the principal site of the bronchiectatic dilatations is justifiable.

Edwards⁴ in a recent article has summarized his indications for lobectomy as follows: "Patients between the ages of 4 and 40 (and

PRECAUTIONS IN THE OPERATING ROOM

In addition to the complications of shock and hemorrhage which may occur during any major operation, the possibility of suffocation from aspiration of pus or blood must be guarded against in all intrathoracic procedures. This is a particularly potent danger in cases of bronchiectasis, where it is almost impossible to avoid squeezing pus out from the bronchial dilatations when the lung is manipulated during the course of the operation. In the majority of instances aspiration through the intratracheal catheter through which the anesthetic agent is administered will keep the airways open. There are occasions, however, when sudden flooding of the tracheobronchial tree by pus or blood will necessitate emergency bronchoscopy. In a few cases where almost constant flooding of the tracheobronchial tree has occurred, we have administered the anesthetic through the bronchoscope, aspirating as often as necessary until the operation was completed. A few minutes' delay in cleaning out the trachea and bronchi may result in the death of the patient. It is necessary, therefore, to have immediately available in the operating room equipment for bronchoscopic aspiration and a capable bronchoscopist. By far the most satisfactory plan is to have a member of the operating team other than the surgeon capable of performing bronchoscopy. This arrangement will enable the surgeon to remain at the operating table and to continue with the operation without delay when the patient's respiratory embarrassment is relieved.

In our own clinic we have adopted a routine for lobectomy cases which includes bronchoscopic aspiration immediately before and after operation. The purpose of the first aspiration is to remove as much of the pus from the diseased lung as possible, the second to evacuate any spillover of blood or pus to the contralateral lung which may have occurred during the operation. It is significant that since adoption of this program about two years ago we have not had a death from post-operative pneumonia or spillover infection in cases subjected to lobectomy.

The simple expediency of being prepared for serious hemorrhage in all thoracic operations will eliminate, except in unusual instances, the danger of fatalities from this complication. Actually, severe bleeding rarely occurs during the performance of lobectomy, but when it does a few moments' delay in replacing the blood spells calamity. It is our custom, therefore, to insert a needle in an ankle vein before the operation is begun through which a continuous flow of physiologic saline or 5 per cent glucose solution may be maintained during the course of the operation (Fig. 3). Compatible citrated blood is available in the operating room and may be given through the

pneumothorax in the future may be reserved for cases subjected to pleural poudrage, a procedure which will be included in the discussion of operative technique.

ANESTHESIA

The ideal anesthetic for intrathoracic operations should furnish first, and most important, a practical means of controlling intrapulmonic pressure; second, facilities for aspirating the respiratory passages during the course of the operation; and, third, rapid return to consciousness on the part of the patient to prevent abolishment of the cough reflex for an extended period of time. Intratracheal administration of the anesthetic insures a stable intrapulmonary pressure and a means for aspirating the trachea. Cyclopropane gas provides the rapidly reversible type of anesthesia.

The introduction of cyclopropane by Lucas and Henderson³² and the work of Stiles and co-workers,³³ which established it as a reliable and safe anesthetic agent, constitute one of the real advances in thoracic surgery. This gas answers practically all of the anesthetic problems peculiar to thoracic surgery. In addition to the advantages which have been enumerated, the ability to administer a high percentage of oxygen, or, if necessary, helium, with cyclopropane (60 to 70 per cent oxygen) permits a satisfactory depth of anesthesia and eliminates the anoxic states which in the past were so common when nitrous oxide or nitrous oxide-ether anesthesia was employed. The only disadvantage of cyclopropane is that the gas is explosive, and the possible advantage of diathermy or the canterly must be sacrificed when it is used.

There have been many improvements and modifications of the original Meltzer-Auer technique of intratracheal anesthesia, which consisted of alternate insufflation of the lungs under hyperpressure. The most objectionable feature of this method was the strong positive pressure which was employed and the virtual standstill of the lungs between insufflations. Defrise³⁴ has advocated what he terms a spiropulsator which permits rhythmical increase and decrease of intrabronchial pressure during anesthesia, and recently Crafoord³⁵ has introduced an anesthesia machine which provides for automatized controlled respiration. These and other inventions have improved the methods of delivering the anesthetic agent and have increased the already wide margin of safety in intratracheal anesthesia.

Lewis,³⁶ Magill,³⁷ and others have reported the successful use of spinal analgesia in lobectomy cases. Pieri³⁸ has employed peridural anesthesia and Burnett³⁹ has recommended local field block. Although it is admitted that patients with sufficiently large vital capacities will tolerate open thoracotomy without the protection of controlled intrapulmonic pressure by intratracheal anesthesia, the deliberate choice of any other method in intrathoracic operations is difficult to understand.

The advantages of having the undiseased portion of the lung held to the chest wall by pleural adhesions have been appreciated for many years, and there have been various types of two-stage operations designed to promote protective adhesions before the lobe was removed. Sauerbruch⁴⁰ inserted paraffin wax on the parietal pleura after removal of segments of several lower ribs in an effort to produce pleural symphysis. Alexander⁴¹ described a two-stage operation in 1933 designed for the same purpose. In the first stage three ribs, the intercostal bundles, and the parietal pleura were excised, the affected lobe was freed, and the pleura was gently wiped with gauze. The second stage was performed ten to fourteen days after the first stage. Churchill,¹⁷ in 1937, recommended a two-stage operation which involved resecting a portion of the eighth rib and division of the adhesions over the affected

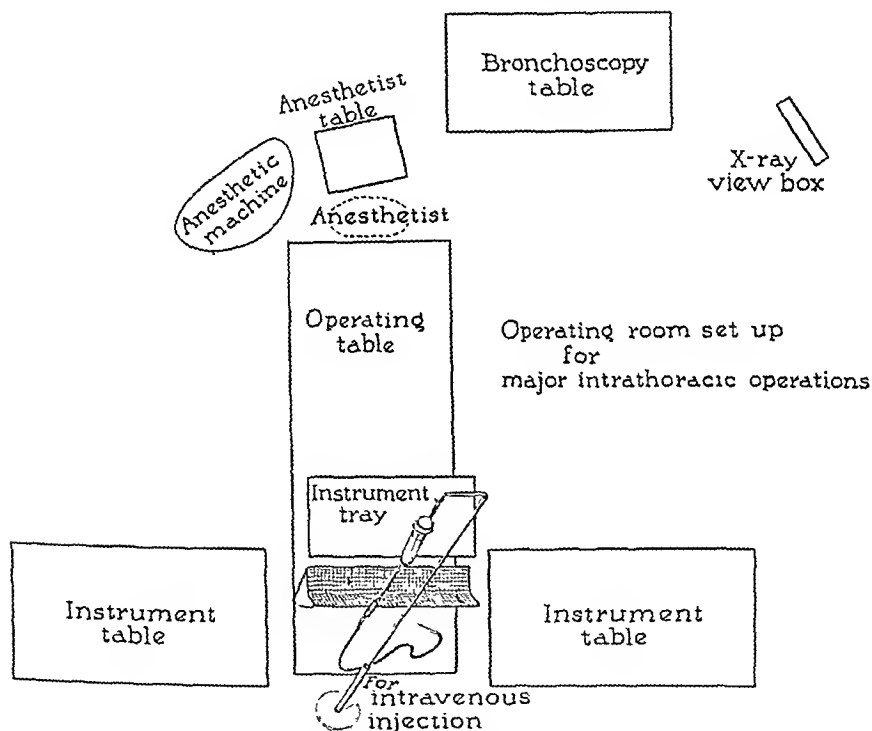


Fig. 4.—Diagrammatic sketch of operating room containing the equipment necessary for major thoracic operations.

lobe. The parietal pleura in the vicinity of the upper lobe was wiped with gauze and the chest closed without drainage. The second stage was postponed for several weeks, and in some instances for months. This delay is, in Churchill's opinion, of great importance, because the patient is given sufficient time to recover from the effects of a major operation, and, moreover, considerable time is necessary for the formation of pleural adhesions of proper density and strength. Monod and

same apparatus whenever necessary. The few instances of severe hemorrhage which we have encountered during the performance of lobectomy have been controlled satisfactorily by this method.

TECHNIQUE OF LOBECTOMY

At the present time, it is impossible to designate the preferred technique for lobectomy, and it is hazardous to predict the method which will be in favor five or ten years from now. There is, however, an increased tendency to employ single-stage operation as contrasted to the

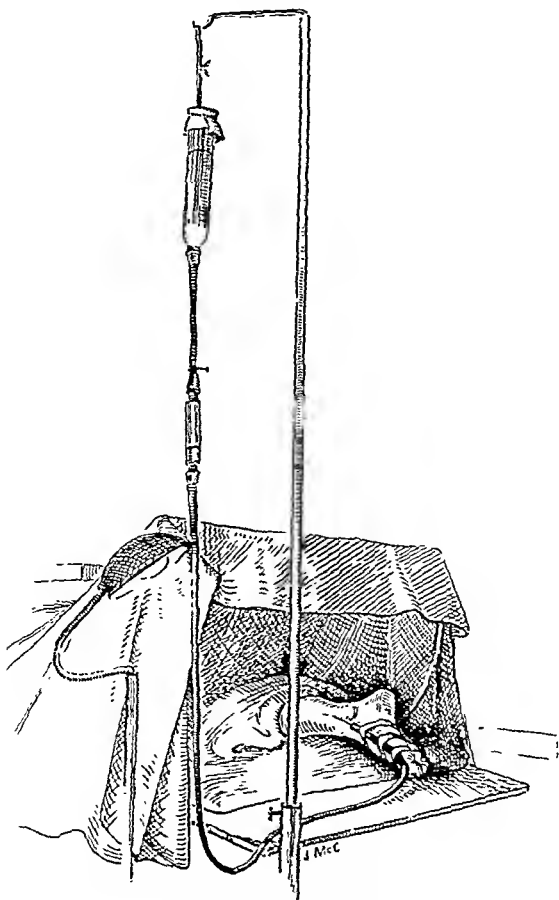


Fig. 3.—Drawing showing arrangement for the administration of intravenous fluids into an ankle vein.

situation a few years ago, when the operation was usually divided into two or more stages. Methods which involve the exteriorization of the diseased lobe which was allowed to slough away gradually have been abandoned generally in favor of clean surgical resection of the diseased portion of the lung.

chiefly: (1) decreased danger of serious hemorrhage; (2) the ability to perform the operation rapidly in subjects who are poor risks; (3) avoidance of the tedious dissection through indurated, infected tissue. The disadvantages are mainly the results of mass ligation of a rather large pedicle of tissue. Fortunately, the low blood pressure in the pulmonary circulation (about 30 mm. mercury) minimizes the danger of secondary hemorrhage, and from the standpoint of reliable hemostasis individual ligation of the blood supply to the lobe is not necessary. Permanent closure of the bronchus, however, constitutes an entirely different problem, and it is in this respect that mass ligation is far from satisfactory. A leak in the bronchus immediately or soon after the operation is serious. Actually, this rarely occurs, and, when a fistula develops late in the postoperative course, the danger to the life of the patient is slight. Empyema thoracis is inevitable, however, if the bronchus does not remain closed. The importance of preventing infections of the pleura following lobectomy can best be emphasized by stating that during the past two years every death from lobectomy which has occurred in my own cases has been the result of a putrid, necrotizing empyema.

It is appropriate at this time to include a word concerning the treatment of empyemas which may complicate lobectomies. With the exception of adequate and early drainage of the pleura, we have been unable to find any effective way to check such infections. At the suggestion of E. A. Graham, blood serum from patients who had recovered from similar infections has been given intravenously and intramuscularly for the purpose of providing protective antibodies. There was no beneficial effect. Chemotherapy in the form of sulfanilamide, sulfapyridine, and lately sulfamethylthiazol has not altered the severity or duration of the infections.

The high incidence of permanent closure of the bronchus and absence of empyemas in instances of total pneumonectomy accomplished by separate ligation of each structure in the pulmonary hilum has stimulated us to apply individual ligation technique to cases of lobectomy, and in 11 consecutive cases in which this method was employed we are privileged to report that only 5 patients developed empyemas. None of the infections was of the putrid variety. Minute bronchial fistulas could be demonstrated in these same patients only by irrigating the empyema cavity with saline solution, and in all instances the fistulas closed within two weeks. These results are encouraging, but more experience with the technique is necessary before final conclusions are drawn. Certainly there will be cases in which adhesions and induration at the root of the lobe will preclude an attempt to dissect out each structure. Speed must be sacrificed if the dissection is carried out, and, when emergencies demand the rapid completion of the operation, mass ligation with a tourniquet is desirable. We feel, however, it is fair

Bonniot,⁴² Churchill,¹⁷ and others feel that the choice between a one-stage or two-stage procedure will depend upon the individual case. Included is Monod's summary of the indications for one- and two-stage lobectomy:

One-Stage Operation: (1) Obliterated pleural space. (2) Operations on children. (3) Middle lobe lobectomy. (4) Severe hemoptysis. (5) Lobar atelectasis. (6) Draining thoracotomy sinus or broncho-cutaneous fistula. (7) Cutting into infected lung when freeing adhesions. (8) Bronchial stenosis.

Two-Stage Operation: (1) Adults with free pleura. (2) Febrile patients with active pneumonitis. (3) Patients treated for a prolonged period with artificial pneumothorax and not having adherent upper lobe. (4) Bilateral cases with free pleural space.

The necessity of performing intrathoracic operations in multiple stages to decrease operating time and thereby lessen the danger of shock or asphyxiation has been practically eliminated by improved anesthetic technique and proper preoperative preparation. The choice between single- and multiple-stage lobectomy will depend, therefore, upon whether or not the value of protective pleural adhesions justifies a major operation to produce them. It is entirely possible that this controversial point will never be settled, as it now seems probable that the comparatively innocuous procedure, pleural poudrage, will prove a safe and effectual method of producing pleural adhesions.

Pleural poudrage was first performed on animals by Bethune⁴³ in 1935. He found that magnesium silicate to which 0.5 per cent iodine had been added (BPC Tale) dusted on the pleura through a bronchoscope would create satisfactory adhesions. Gowar⁴⁴ in England has recently investigated the problem of pleural poudrage, using a wide variety of chemical irritants on the pleura. He concluded that the powder originally used by Bethune is entirely satisfactory and can be employed safely. The operation has been used by Edwards preliminary to lobectomy in 8 adults, and he feels that the effects have been beneficial in every instance. The procedure is receiving an extensive trial by those who place a large premium on protective pleural adhesions, and it is safe to predict that, in the future, pleural poudrage will supplant open thoracotomy as the first stage in two-stage lobectomy.

Interest in single-stage lobectomies was revived in 1929 by Bruhn⁴⁵ who reported 6 cases with 1 death, and his experiences stimulated others to attempt operations in the free pleura without protective adhesions. The tourniquet, designed by Shenstone and Janes⁴⁶ to control the hilum of the lobe until the structures were secured by sutures, added to the popularity of the one-stage procedure, and in the majority of clinics today the technique most frequently employed is probably that of mass ligation of the hilum of the lobe with the aid of a tourniquet, performed in a single stage. The advantages of the tourniquet technique are

to assume that, when feasible the individual ligation technique for lobectomy has distinct advantages over mass ligation, by insuring better bronchial closure and reducing the incidence of postoperative empyemas (Fig. 5).

One of the most important advances in the technique of partial or complete pneumonectomy has been the perfection of methods by which it is possible to remove all or part of the lung without producing visible deformity of the chest wall. It is no longer considered necessary to resect portions of several ribs to obtain adequate exposure for intrathoracic operations, and the division of two or three ribs near their posterior attachments or the resection of one rib will, except for rare instances, furnish splendid exposure for lobectomy. Fig. 6 reveals the contrast in the appearance of the chest wall of the patient operated upon twenty years ago for lower lobe bronchiectasis and one on whom modern technique was employed.

POSTOPERATIVE CARE

The postoperative care of a patient who has been subjected to lobectomy involves attention to the same details which are important following any major operation. During the first six or eight hours after the operation, pulse and blood pressure readings must be checked frequently and, if there is any tendency toward shock, a transfusion of blood should be given. In addition to these precautions it is important that the patient be encouraged to cough as soon as he reacts from the anesthetic. Although it is not absolutely necessary, the routine use of an oxygen tent is desirable because the immediate postoperative discomfort is decreased by the constant, cool, oxygen-rich environment. The necessity for frequent change of position must be emphasized to the nursing staff. It is our custom to keep the patient on his back or with the side which has been operated upon down until all the effects of the anesthesia have disappeared. These same positions are encouraged throughout the postoperative course when the patient is sleeping, for, in case the bronchus should open suddenly, fluid might be aspirated to the contralateral lung while the patient is unconscious. The catheters which have been inserted into the chest at the time of operation should be inspected at least twice a day to be sure that they are open and functioning properly. The catheters are gradually shortened throughout the postoperative course and, in the uncomplicated case, can be withdrawn in three or four weeks. Patients are usually allowed to be out of bed within three weeks, depending, of course, upon the condition of the individual case.

SUMMARY

In a period of less than ten years the mortality rate of lobectomy for bronchiectasis has decreased from approximately 50 per cent to less than 10 per cent. In contrast to the questionable clinical results ob-

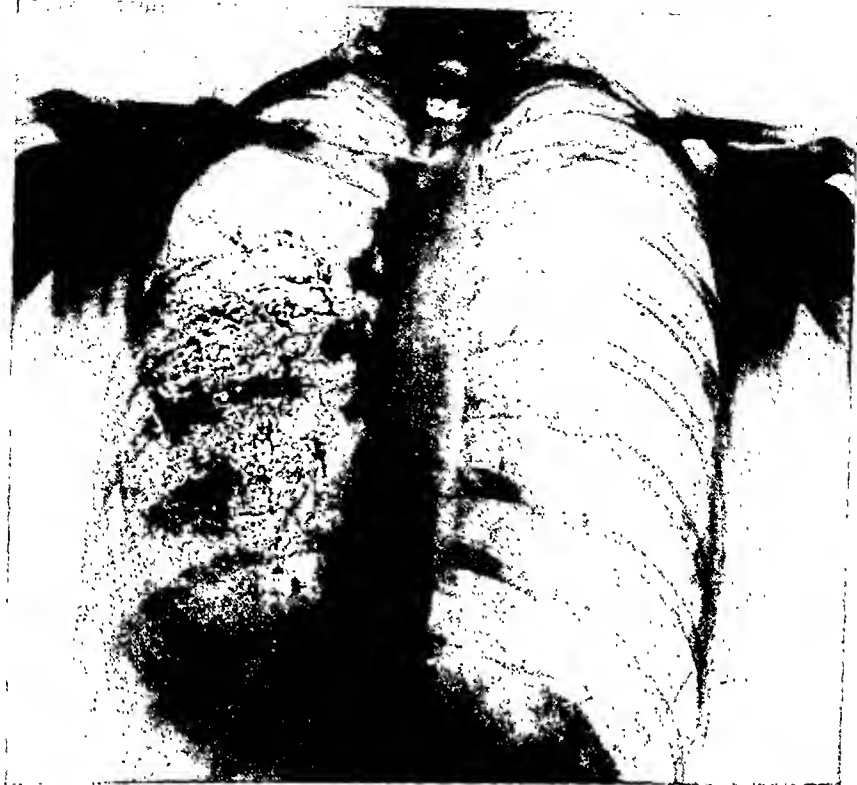


Fig. 5.—Postoperative lipiodol bronchogram after right lower lobe lobectomy by individual ligation technique. Note complete absence of residual bronchial stump. There was no postoperative empyema.



Fig. 6.—Improvements in the cosmetic result of lobectomy are noted by contrasting two patients operated upon by E. A. Graham, one (A) who had his operation twenty years ago, and the other (B) who had a lobectomy in 1933. No ribs are now removed and there is therefore no deformity of the thorax.

Book Reviews

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The author has introduced several original and effective methods of presentation. The book is profusely illustrated, for the most part by the author's own drawings. These are mainly directed toward the illustration of mechanical problems. In particular, the mechanism of labor is presented by means of illustrations which are effective and make the usual verbal descriptions seem poor by comparison. The use of outlines of the subject material to follow will aid the undergraduate student in grasping the problem as a whole.

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tained by the operation a few years ago, excellent results can now be anticipated when lobectomy is employed. The remarkable advances which have occurred are not dependent on refinements in operative technique or any other single factor, but have been the result of a combination of improvements in anesthesia, proper preoperative localization of the disease, and certain preoperative and postoperative precautions which have been described.

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In the preface to the fifth edition the author states that he has deliberately refrained from changing the pagination of the text, ever since the appearance of the first edition. He thereby implies that our knowledge of the various subjects in surgery, or their importance, does not change enough as the years roll by to warrant changing the amount of space devoted to these subjects. Other examples of maldistribution of space are noted. For example, the discussion on wounds is limited to six pages in the chapter on surgical technique, except for additional data scattered throughout the book in areas where they are not readily found. The reviewer is inclined to believe that the subject of wounds is sufficiently important to deserve consideration in a separate chapter. One and one-half pages are devoted to typhoid fever and only two and one-half pages to tetanus. In the discussion of tetanus no mention was found of the use of active immunization—a subject so very important in these Martian times. Surgeons in the southern climate might object to devoting only one-half page to lymphopathia venereum.

The chapters on blood vessels and lymphatics are very well done, as are also the chapters on anesthesia and amputations, which represent material added since the first edition. Surgery of tuberculosis is discussed in a splendid manner.

The chapter on intestinal obstruction is not up to the standard of the rest of the book. The reviewer would criticize the author's weak acceptance of the value of Wangenstein suction in the treatment of intestinal obstruction. Doubtful acceptance would not have been so inappropriate a few years ago when it was first introduced, but the frequent reports of such radical reductions in mortality by its use would appear to establish it as a definite aid in the treatment of intestinal obstruction. In the discussion of methods of intestinal decompression many surgeons, indeed, would object to the statement or question appearing on page 938, reading as follows: "For if they are to replace operation, how is it known that, in any case, strangulation of intestine is not present?" The authors writing on the subject of intestinal obstruction do not appear to have that much difficulty in determining the presence or absence of strangulation.

In the discussion of posterior operation for carcinoma of the rectum on page 986, a statement is made, the latter half of which reads as follows: "(Lockhart-Mummery) carries a low mortality but leaves behind such cancerous nodes as are associated with the proximal portion of the superior hemorrhoidal artery (page 969) not a very serious disadvantage." This is presumably a misprint, the word "not" being included by error. If not, the statement requires supporting data.

Remarkably few misprints or misstatements are found. For this accomplishment the author is to be congratulated. As a whole the book is splendid and will be a valuable one for use by the student or teacher.

Principles of Surgical Care: Shock, and Other Problems. By Alfred Blalock, M.D. Pp. 323, with 13 illustrations. St. Louis, 1940, The C. V. Mosby Co. \$4.50.

There is probably no one so well equipped to write a monograph on shock as is Blalock, and he has lived up to expectations in presenting a book which every student and every practitioner of medicine should have. Although shock is the principal theme of the monograph, those factors which predispose to the development of shock and which, if prevented, will prevent shock are adequately discussed. A particularly important chapter as regards this point is that on anesthesia and anesthetic agents. The chapter on shock is superbly done with a complete review of the literature. The author's own fundamental investigations and a review of 246 references give a résumé on this subject which is thoroughly complete. Of

great importance in the care of patients preoperatively and postoperatively is the determination of metabolic and nutritional disturbances and their correction by the administration of fluids and electrolytes. This is well discussed from the physiologic and physiochemical aspects. Other postoperative disturbances, such as nutritional disorders, including vitamin deficiencies and endocrine deficiencies, as well as postoperative pulmonary and abdominal complications, are thoroughly considered. Throughout the book the physiologic aspect is always foremost and the rational consideration of each condition is discussed. Last, but certainly not least, one of the most valuable parts of the entire book is the very complete bibliography. Few monographs are so completely done. Because of the completeness of the work and because of the author's vast experience with the subject, this book should be in the library of every student and practitioner of medicine.

Minor Surgery. By Frederick Christopher, M.D. Ed. 4. Cloth. Pp. 990, with 639 illustrations. Philadelphia, 1940, W. B. Saunders Co. \$10.

To those familiar with the previous editions of this book no recommendation is necessary, other than to say that the fourth edition is a worthy successor to its predecessors. This last edition comprises 990 pages and is abundantly illustrated with both photographs and drawings. The subjects discussed include many things which are not usually classed as minor surgery. For example a rather extensive survey of the treatment of fractures is given. As is stated in the preface, however: "The subject matter deals with those procedures which comprise numerically the bulk of all surgical procedures, the ones carried out by the general practitioner, the physician who does not have ready access to a large hospital or contact with surgical specialists, the younger surgeon, the resident surgeon and the intern." This is an eminently practical book. It will often be referred to when those more or less simple conditions, the proper care of which may have been crowded from the doctor's memory by more complicated and serious matters, are under consideration. Throughout the book emphasis has been laid on treatment and technique. The printing in small type of many paragraphs concerned with technique has made it possible to include an unusual amount of detail and certainly increases the value of the book. Included at the bottom of appropriate pages are 268 references to original articles in the recent medical literature. Practically all the newer concepts of surgical treatment have been included to bring the treatise completely up to date. These include the various methods of handling wounds, the administration of intravenous anesthetics, peritoneoscopy, vitamin therapy, water and electrolyte balance, and intermittent venous occlusion.

However specialized or however experienced the surgeon may be, he will find much in this book which will be valuable to him.

Operative Surgery. Ed. 5. By J. Shelton Horsley, M.D., and I. A. Bigger, M.D. 2 vols. Pp. 1567, with 1,391 illustrations. St. Louis, 1940, The C. V. Mosby Co. \$18.

The fifth edition of Horsley and Bigger's *Operative Surgery* has been changed considerably and has been modernized to include many of the newer procedures which make the book valuable for the student and the surgeon. Such operations as ligation of the patent ductus arteriosus, extrapleural pneumothorax, and many other new ones have been included in this edition. The book is well illustrated and is well written both from the standpoint of description and from the standpoint of reasoning.

In discussing complications of operations in the sections on shock and hemorrhage, the uses of sulfanilamide and sulfapyridine are adequately described. The chapter on continuous intravenous injections is particularly well done, as could be easily imagined because of the interest which the senior author has had in this subject. In it are included the importance of preventing hyperproteinemia and also the newer use of alcohol as an infusion. The chapter on transfusions is not particularly well done, and it is regrettable that the semidirect method by means of a cannula is even described at all. The chapter on suturing blood vessels is very well done; in fact, it is probably more detailed than is necessary for a work of this kind. However, it is difficult to understand why, after such an elaborate description of arterial suture, nothing is said of the use of heparin in such cases to prevent thrombosis. Although the chapter on aneurysms is adequately described, nothing is given concerning the method of developing collaterals in aneurysms, either by means of the Matas compressor or by the newer method of treating the collaterals by means of blocking the sympathetic impulses. The chapter on plastic surgery in general. The remaining chapters are well done. The chapter on neurosurgery by Coleman is splendidly handled and leaves nothing to be desired. The volumes are valuable and should be in the library of every surgeon. It is unfortunate that more complete bibliographies are not given at the end of each chapter, as this would make the work even more valuable for the student.

Injuries of the Skull, Brain and Spinal Cord. Samuel Brock, M.D., Editor. Cloth. Pp. 632, with 63 illustrations. Baltimore, 1940, Williams and Wilkins Co. \$7.

This monograph edited by Brock contains twenty-two chapters on different phases of the subject, each contributed by different authors who have been especially interested in the particular phase. Like most, if not all, monographs compiled in this manner, this book is well written and quite completely covers the subject of injuries of the skull, brain, and spinal cord. It is not permeated by the opinion or practices of one individual, but summarizes the literature and the personal experiences of the authors. This book is the most complete and best text in English on the subject.

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SURGERY

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Original Communications

CONGENITAL PREPYLORIC MEMBRANOUS OBSTRUCTION IN A PREMATURE INFANT*

ARTHUR S. W. TOUROFF, B.S., M.D., AND RALPH M. SUSSMAN, M.D.,
NEW YORK, N. Y.

*(From the New-Born Service of the Jewish Maternity Hospital and the Pediatric
and Surgical Services of Beth Israel Hospital)*

INTRODUCTION

AUTHORITIES^{2, 11, 14} agree that, exclusive of hypertrophic pyloric stenosis, congenital obstructions of the stomach are very rare; Pfaundler and Schlossman¹¹ state that they are so uncommon as to have no special significance. According to von Reuss¹⁴ such lesions, classified by most authors as atresias and stenoses, are found exclusively at the pylorus. Anders,² however, states that they may involve the cardia and fundus as well.

Anders² is of the opinion that congenital obstructions of the cardia can occur only in the form of septa, similar to those noted occasionally in the esophagus, but cites no cases from the literature. He states that only two cases of congenital occlusion of the body of the stomach have been reported, one by Aregger and the other by Wendel. In the first, obstruction was due to a band of mucous membrane which sprang from the pyloric region in association with hypertrophic stenosis of the pylorus. In the second, the lumen of the stomach was divided by a cystic tumor derived from an accessory pancreas imbedded in the wall of the stomach near the pylorus. Although only a single case of congenital hourglass stomach has been reported (Saake), it is the opinion of Anders² that the lesion in question was not of congenital origin. Sternberg and Klose (quoted by Anders) concur in this view and doubt the existence of congenital hourglass stomach. Von Reuss¹⁴ states that he has observed only one case of pyloric atresia, and that Kreuter was able to collect only four cases from the entire literature. Anders² emphasizes that, because

*Presented before the joint meeting of the New York Surgical Society and the Philadelphia Academy of Surgery, Feb. 8, 1939.

Received for publication, Feb. 20, 1940.

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The illustrations are well reproduced. Each chapter is accompanied with its own bibliography; many of these bibliographies are quite extensive.

For ready reference, this is the best book available on the subject.

pyloric sphincter "unusually developed." A posterior gastroenterostomy was performed, but the child died seventeen days later. At post-mortem examination the pyloric sphincter was markedly hypertrophied, but, in addition, the mucous membrane of the greater curvature of the stomach, at the entrance to the pylorus, was duplicated in such a fashion as to form a flap which closed the pylorus completely when attempts were made to force fluid from the stomach into the duodenum. When fluid was caused to flow from the duodenum toward the stomach, however, the mucous membrane flap was forced back into the stomach and thus offered no resistance to the passage of the fluid. The unusual anatomical findings described above explained why bile entered the stomach and appeared in the vomitus in the presence of complete pyloric obstruction. Whether the obstructing flap was merely a redundant fold of mucosa, such as is commonly encountered within the pyloric lumen in cases of hypertrophic pyloric stenosis, or whether it represented a separate congenital anomaly is difficult to state. Since an extensive review of the literature has failed to reveal a case similar to the one about to be reported, it appears warranted to present the latter in detail.

CASE REPORT

B. L., a white female infant, was born at the Jewish Maternity Hospital, New York, N. Y., on Sept. 11, 1938. This date was approximately four weeks in advance of the completion of full term. The mother, a native-born woman, 38 years of age, whose pregnancy was complicated by marked polyhydramnios, went into labor spontaneously and was delivered without difficulty six hours later by one of us (R. M. S.). Her only other pregnancy, seven years previously, also had resulted in the birth of a premature child who suffered continuous cyanosis and died on the third day of life. No post-mortem examination was performed but, in view of the paternal family history about to be presented, the possibility of death from a congenital anomaly must be considered.

The infant's father, who was one of three siblings, had two sisters. Each of the latter bore only a single child. Both of these children died in infancy, one of cerebral agenesis and the other of mongolism. Thus, three and possibly all four offspring (including B. L.) of the patient's father and his two sisters suffered from some congenital anomaly. Accordingly, it is warranted to assume that the developmental defect observed in B. L. was of paternal origin. Another possibly related factor was the existence of marked polyhydramnios during the mother's pregnancy. The frequent association of this condition with congenital anomalies and premature birth is well known, and reference concerning it may be found in practically all standard works on obstetrics.¹⁵

At birth, B. L. weighed six pounds and presented no gross external abnormalities. Initial cyanosis, however, was quite marked and responded to intensive treatment only after a period of five hours. No meconium was passed during or after delivery. The child was placed upon a feeding formula, which she took well. Within a short time, however, she began to vomit, the vomiting occurring toward the end of each feeding. This regurgitation appeared effortless and was nonprojectile in character. Various changes in the amount and composition of the formula failed to influence the vomiting appreciably, and it soon became evident that no food was being retained. During the first and second days the child had no spontaneous bowel movements, even of meconium; and an enema administered at

of the difficulty in differentiating at times between acquired and congenital pyloric atresia, the only cases worthy of consideration as of *truly congenital origin* are those encountered during very early life. He states that only three of the latter cases have been reported, two by Hammer and one by Sternberg, and ventures the opinion that they might possibly be explained on the basis of an abnormally high atresia of the duodenum.

Von Reuss¹⁴ divides congenital stenosis of the pylorus into three types. The first is the hypertrophic (Hirshsprung) type, which is too well known to require description. The second is the nonhypertrophic (Landerer-Maier) type, in which the lumen of the pylorus is very narrow but lined by mucous membrane, which is normal except for its thinness. Although this is a true congenital lesion, it seldom produces symptoms during childhood. In most instances the symptoms appear fairly late in life, and operation discloses a pylorus which is narrow without apparent cause. According to von Reuss, only one case of nonhypertrophic pyloric stenosis has been described in an infant. In this case, reported by Schafer, the malformation consisted of a small fistula-like pylorus without a sphincter. The third type of congenital pyloric stenosis mentioned by von Reuss includes connective tissue stenoses and anomalies of formation. These are due to peritoneal bands or adhesions which compress the lumen from the outside and septa of mucous membrane within the lumen. Mya (quoted by von Reuss) believes that the former may originate in fetal peritonitis, while the latter apparently correspond to the congenital occlusions which occur in the remainder of the digestive tract. To von Reuss' three types of congenital pyloric stenosis, a fourth may be added. This is due to compression of the pyloric canal by a tumor, usually a cyst, arising from aberrant pancreatic tissue, imbedded in the wall. Identical in origin with the lesion in the fundus of the stomach reported by Wendel, cysts derived from aberrant pancreatic tissue and occluding the pyloric canal have been reported by Hale,¹⁵ Lyons,¹⁶ Bikoff¹⁷ and others.

Although von Reuss includes septa of mucous membrane in his third group of cases of congenital pyloric stenosis, he cites no cases in which such lesions were found. A personal survey of the literature likewise has failed to reveal a report of such a case. Our interest in this type of congenital occlusion is the result of a recent personal experience in which it was encountered at operation, in a premature infant in whom vomiting commenced at birth. In our investigation of the literature we encountered only one other case in which a barrier of mucous membrane was responsible for obstruction of the pylorus. Although the case bears only slight resemblance to ours, it is of interest. Described by Bonner¹⁸ in 1912, it concerned a 4-week-old infant, who presented symptoms of "intractable pylorospasm" unrelieved by intensive medical treatment. At operation, the stomach was found to be greatly distended and the

therefore, were assumed to be due to air, introduced accidentally with previous enemas. These findings indicated the presence of a complete obstruction, involving either the pyloric portion of the stomach or the very first portion of the duodenum. A film made shortly thereafter (Fig. 2) revealed the structure in question to have become distinctly bilocular. The distal portion now was globular in contour and relatively more distended than previously. It reached down almost to the level of the right iliac crest and was separated from the proximal portion by a well-marked constriction. The findings still were difficult to interpret since it was not clear whether the distal air-filled pouch represented greatly dilated, proximal portion of duodenum, separated from the stomach by the pylorus, or whether it represented a dilated pyloric antrum separated from the body of the stomach by a contraction of the musculus sphincter antri.

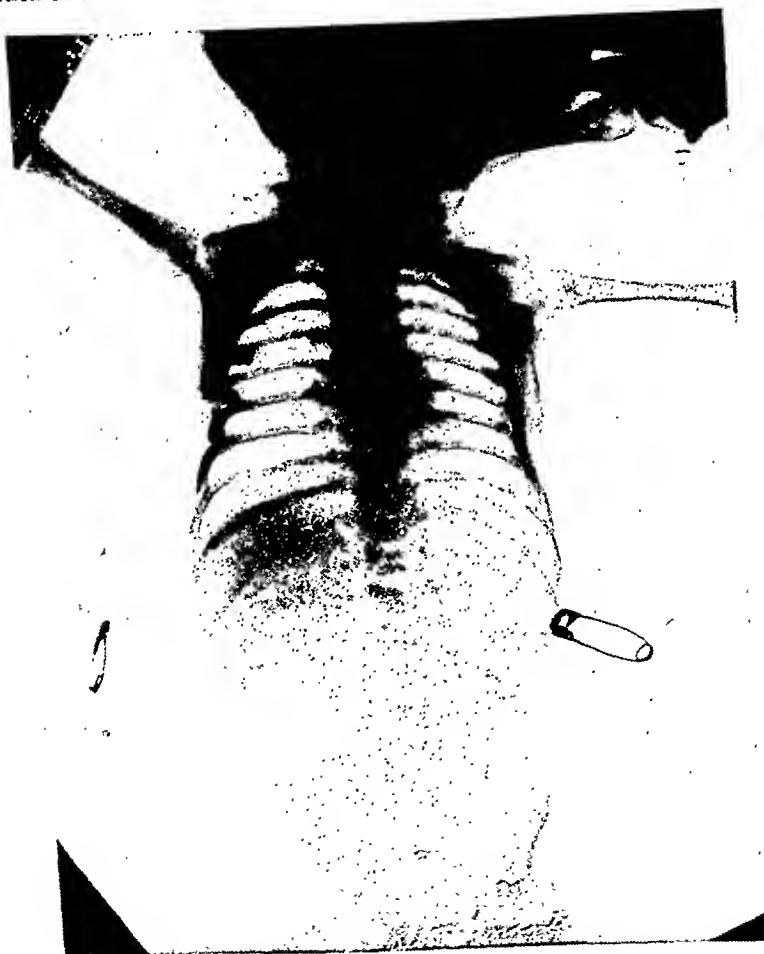


Fig. 2.—Several hours later. Stomach now is bilocular. Distal pouch (antrum) distended and separated from body and fundus by contraction of musculus sphincter antri.

On the fifth day all symptoms continued and the child lost ground steadily in spite of the administration of several transfusions and large quantities of fluid by vein and subcutaneously. At that time the stomach was aspirated, a small amount of thin barium mixture administered by gavage, and x-ray films taken immediately.

the end of the second day resulted in the return of only a small amount of colorless mucus. In spite of this apparent evidence of obstruction of the gastrointestinal tract, the abdomen was not distended. On the third day, because of progressive loss of weight and dehydration and the continuation of obstipation and vomiting, she was transferred to the Pediatric Service of the Beth Israel Hospital. There, the parenteral administration of fluids was begun. In view of icterus, which appeared more marked than was to be expected on the third day of life, the urine was examined for bile and found positive. Examination of the vomitus for bile was negative, as were similar examinations on a number of subsequent occasions.

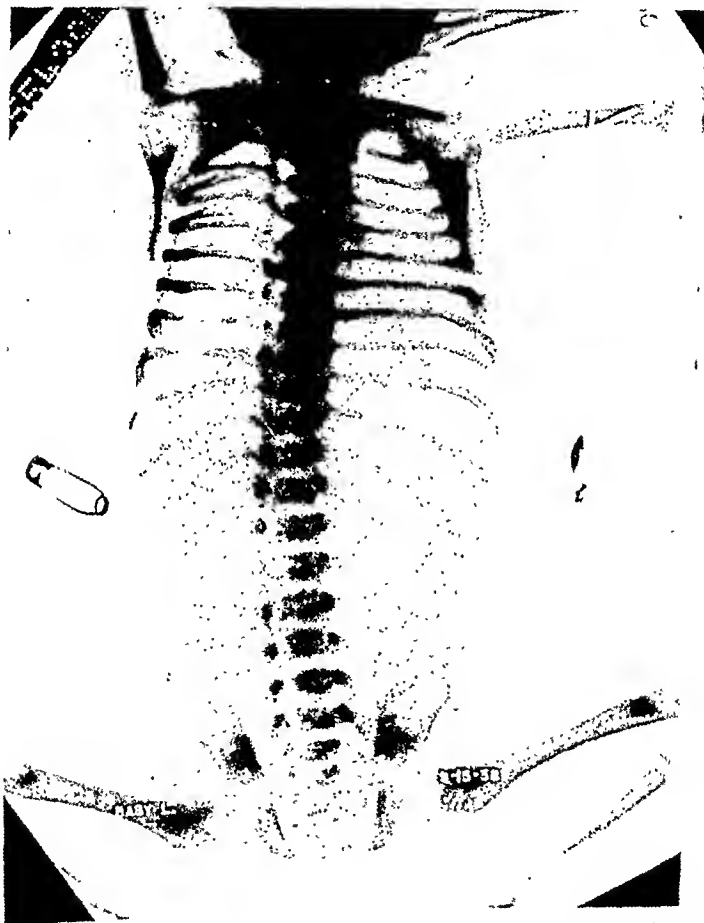


Fig. 1.—Fourth day of life. Stomach diffusely distended. No gas in small intestine. Bubbles in rectum, sigmoid, and splenic flexure are due to air accidentally introduced with previous enemas.

On the fourth day, because of persistent obstipation and vomiting, X-ray examination was performed (Fig. 1). This revealed the stomach to be diffusely distended with air, the body of the viscus extending downward to a point about 1 inch above the level of the iliac crests, and across the midline to the right side of the abdomen. It was uncertain whether or not the first portion of the duodenum formed a part of this air-filled pouch. The small intestine contained no gas, and the few bubbles noted in the rectum and in the sigmoid and splenic flexures of the colon.

pectoral, axillary, and scapular regions as the result of poor absorption of previously administered clyses. (Taking into consideration the volume of this retained fluid, the child's weight undoubtedly was less than 5 pounds.) The mouth, tongue, and pharynx were deeply congested and studded with adherent white patches characteristic of thrush. The abdomen was not distended and was soft throughout. No abdominal masses were palpable and no peristaltic waves were visible. During examination the child vomited several mouthfuls of clear, yellowish fluid. Gastric aspiration yielded 40 c.c. of similar fluid which on chemical analysis contained no bile. The blood count was as follows: R.B.C., 4,200,000; hemoglobin, 160 per cent (due to dehydration); W.B.C., 8,900 with 61 per cent polymorphonuclear leucocytes. The urine contained a trace of bile but otherwise was not remarkable. A rectal irrigation administered at the time, was totally ineffectual.

Discussion of Diagnostic Features.—On purely clinical grounds the continued vomiting, obstipation, and ineffectiveness of enemas since birth five days previously warranted the diagnosis of a congenital anomaly resulting in obstruction of the gastrointestinal tract. The absence of bile in the vomitus on all examinations and the lack of abdominal distention appeared compatible with a very high obstruction involving either the stomach or the duodenum proximal to the papilla of Vater. The very early appearance of symptoms, the sex of the child, and the absence of projectile vomiting, visible peristalsis, and palpable abdominal mass constituted strong presumptive evidence against the diagnosis of congenital hypertrophic pyloric stenosis.

The presence of bile in the urine, in conjunction with icterus which appeared more intense than that usually to be noted on the fifth day of life, could be explained in two ways. The first possibility was that they were merely an accompaniment of prematurity. According to Holt and Howland,⁷ icterus neonatorum may or may not be present in normal newborn infants. These authors state that in premature and delicate infants, however, it occurs regularly and is apt to be more severe and to last longer than normally. They also emphasize that bile, which ordinarily is not present in the urine in mild cases, is apt to be noted in the more severe cases. The second possibility as regards the significance of icterus and bile in the urine, especially in a patient in whom one congenital anomaly already was assumed to be present, was that these manifestations were due to the presence of an additional anomaly such as an obstructive lesion of the biliary duct system. The latter might be either a stenosis due to external pressure or an atresia at some point in the duct system. Biliary obstruction of either of these types, if complete, would have accounted satisfactorily for the absence of bile in the vomitus. Under such circumstances the occlusion of the gastrointestinal tract, discussed above, might have been situated in the duodenum distal to the papilla of Vater or in the uppermost portion of the jejunum. The lack of abdominal distention, however, made it appear unlikely that the obstruction could be situated distally to the latter point.

In the previously described distal pouch, the opaque medium formed a dense, smooth-edged, ovoid shadow, measuring about $1\frac{1}{4}$ by $\frac{3}{4}$ inches. During a short period of fluoroscopy, no barium passed beyond this point. Films made four hours later (Fig. 3) revealed the body and fundus of the stomach to be greatly distended still with air and to contain practically no barium. The dense, ovoid, distal shadow had become larger in size and more circular in contour. Barium still had not advanced beyond this area, indicating conclusively the presence of complete obstruction. Whether the latter involved the first portion of the duodenum or the distal portion of the stomach still was uncertain. However, in view of the persistent obstruction, regardless of its exact site, it appeared warranted to assume that continuation of conservative therapy would be unavailing and surgical opinion, therefore, was requested.



Fig. 3.—Four hours after ingestion of barium. Barium-filled antrum remains sharply demarcated from the air-distended body and fundus by spasm of the musculus sphincter antri. No barium in small intestine, indicating presence of complete pyloric obstruction.

When seen in consultation by one of us (A. S. W. T.) on the afternoon of the fifth day, the temperature was normal. Pulse and respiration were too rapid to count with accuracy. Jaundice was fairly deep, and there was evidence of moderate dehydration. The weight was 5 pounds, 4 ounces (a loss of more than one seventh of the birth weight). Considerable local swelling and edema were present in the

to the dilatation of the antrum, the site of the pyloric ring was further marked by a relative, slight external constriction. As the result of the marked downward and lateral displacement of the enlarged antrum, the first portion of the duodenum had become considerably elongated and coursed upward quite sharply for a distance of about 1 inch to reach the region of the head of the pancreas. The second and third portions of the duodenum were visualized indistinctly.

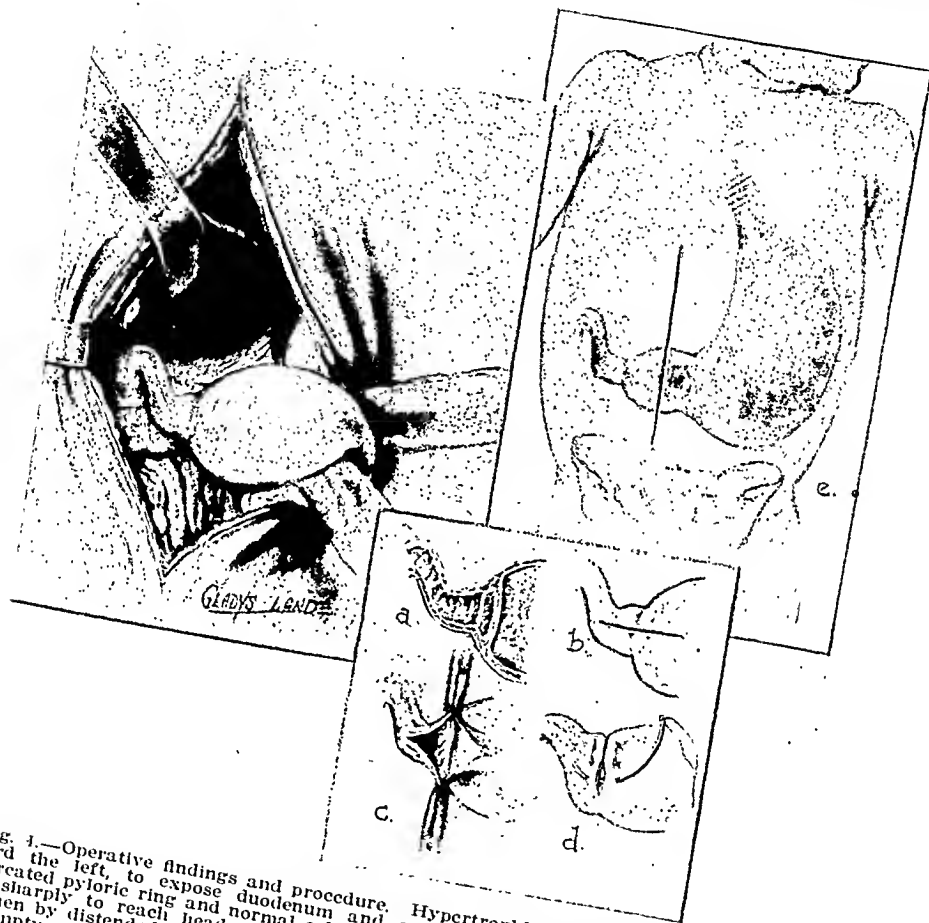


Fig. 1.—Operative findings and procedure. Hypertrophied dilated antrum retracted toward the left, to expose duodenum and gastroduodenal junction. Note sharply demarcated pyloric ring and normal caliber of duodenum. Duodenum is elongated and rises sharply to reach head of pancreas. Entire liver displaced into right side of abdomen by distended stomach. Large bowel almost completely hidden. Small intestine empty and contracted. a, Cross section of antrum and adjacent duodenum showing site of mucous membrane septum in immediate prepyloric area; b, incision through proximal portion of duodenum and adjacent stomach; c, incision about to be closed at right angles to its original direction (Heineke-Mikulicz pyloroplasty); d, pyloroplasty continued; inner (continuous) suture completed; outer tier of mattress suture being placed; e, diagrammatic sketch of site and extent of incision.

No external peritoneal bands or folds were present at any point on the surface of the stomach or duodenum, thus ruling out external constriction as the cause of obstruction. Since the stomach was distended, the pyloric ring clearly visible, and the duodenum normal in caliber, it was evident that the obstruction was due to an intrinsic lesion situated in the distal portion of the stomach. To prove this point, the proximal portion of the stomach was compressed manually in order to force its contents distally. As this was done, the antrum became tensely bal-

The complete absence of the passage of meconium or stool at any time during life could be explained in two ways. The first was by the presence of still another anomaly, an obstruction involving the lower bowel. The second explanation was that offered by Alvarez,¹ who pointed out that the best stimulus to intestinal peristalsis is the passage of gastric contents through the pylorus into the duodenum. In accordance with this theory the presence of complete pyloric obstruction alone could account for the failure of our patient to pass meconium.

Roentgenographic examination confirmed the clinical impression of a high, complete obstruction, which, for reasons to be discussed later, appeared to be intrinsic in nature. The exact site of obstruction, i.e., either in the very first portion of the duodenum or in the distal portion of the stomach, was uncertain although the latter appeared more likely. The examination offered no information in regard to the question of an obstruction of the biliary passages and shed no light on the problem of the existence of an additional low intestinal obstruction as seemed quite possible from the failure of the child ever to pass meconium.

Regardless of the presence or absence of anomalies in addition to the high complete obstruction, immediate operation was advised, for the reason that the child was starving in spite of parenteral feeding and death seemed inevitable unless the obstruction were relieved. Because of the patient's prematurity and generally poor physical condition, a bad prognosis was given.

Operation.—On Sept. 16, 1938, under open ether anesthesia the abdomen was opened by one of us (A. S. W. T.) through a $4\frac{1}{2}$ inch right paramedian, musculo-splitting incision, which extended from the right costal arch to a point below the level of the umbilicus (Fig. 4e). The stomach, which was greatly enlarged, presented in the wound at once. On exploration it was found to occupy most of the left half of the abdomen, from the diaphragm almost to the level of the iliac crest, and to extend across the midline to the right side. In the latter region its upper half was covered by the free margin of the liver. The latter organ, which was about one-half the size of an adult's fist, was found displaced entirely into the right side of the abdomen by the distended fundus and body of the stomach (Fig. 4). On retracting the margin of the liver upward and laterally and drawing the proximal portion of the stomach to the left, the upper half of the distal portion of the stomach and the first portion of the duodenum were exposed. The edges of the wound then were retracted widely and the major portion of the stomach visualized. The viscus measured about 5 by $2\frac{1}{2}$ inches in its greatest diameters, the fundus and body being demarcated from the antrum by a fixed contraction (spasm) of the musculus sphincter antri which, in effect, divided the organ into two pouches. The proximal pouch, consisting of the body and fundus, measured about 3 by $2\frac{1}{2}$ inches in diameter. Its walls were judged to be of normal, or perhaps slightly less than normal, thickness. It was distended with air and fluid, but could be indented readily. The distal (antral) pouch measured about $1\frac{1}{2}$ by 2 inches in diameter and was roughly globular in shape. Its walls were appreciably thicker and more resistant to pressure than those of the proximal pouch. As the organ was handled, the muscular contraction between the two pouches relaxed somewhat. The duodenum measured about $\frac{1}{4}$ inch in diameter, its most proximal portion widening slightly as it joined the dilated antrum. The junction of the stomach and duodenum was clearly marked by the pale, glistening pyloric ring. Due

gastric wall. In order not to narrow the lumen of the gastroduodenal junction or the duodenum, a Heineke-Mikulicz pyloroplasty was performed by closing the existing horizontal incision in a vertical direction (Fig. 4c and d). Two layers of sutures were employed for this purpose: an inner, continuous Connell stitch of No. 000 chromic catgut, reinforced by an outer tier of interrupted No. 000 chromic mattress sutures. After the incision had been closed, gas and fluid could be milked readily from the stomach into the duodenum. In order to terminate operation as quickly as possible, the abdomen was closed with interrupted through-and-through sutures of heavy silk, which approximated the structures of the abdominal wall in one layer.

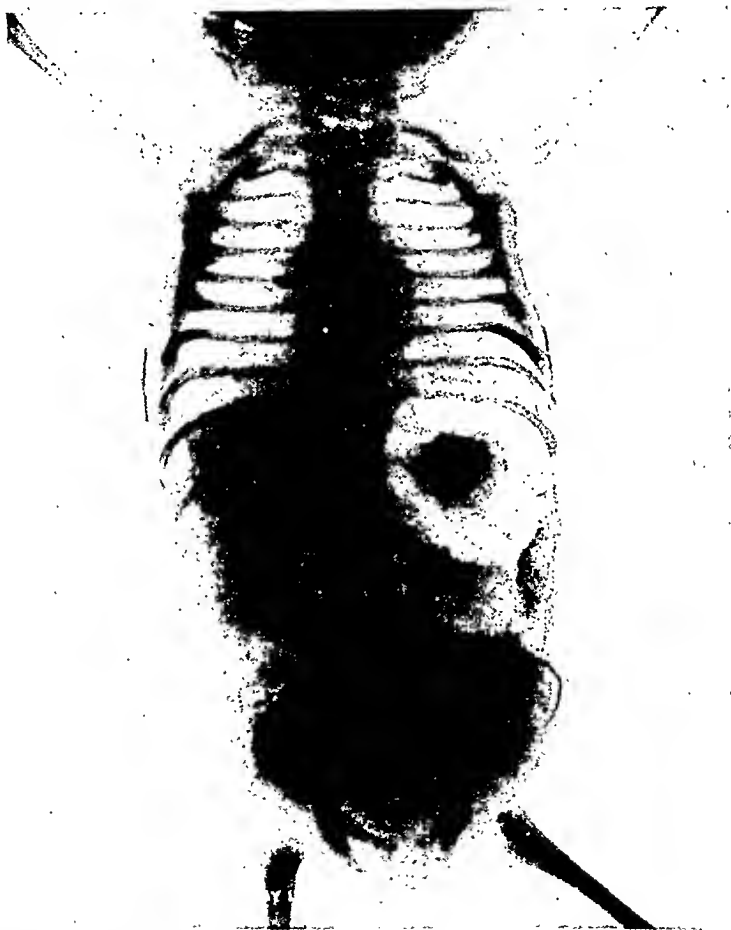


Fig. 5.—Two days postoperatively. Stomach still bilocular, but smaller. Antrum now situated in front of vertebral column. Note gas-filled first portion of duodenum, shaped like reversed letter S, immediately beyond the antrum. Gas also present in intestine below duodenum.

Postoperative Course.—Although the immediate postoperative reaction was satisfactory, a prophylactic transfusion of 60 c.c. of citrated blood was administered the same night. At the end of six hours, feedings of 5 c.c. of glucose in Ringer's solution were given every half-hour. Periodic postoperative vomiting occurred during the first twenty-four hours, but the major portion of the feedings were retained. The vomitus now (for the first time) contained bile, indicating patency

looned with gas and fluid, but the caliber of the duodenum did not change in the slightest degree. The site of obstruction thus having been established at the pylorus, the abdomen was rapidly explored for evidence of other anomalies. The other viscera because of their small size are worthy of brief description. The gall bladder, which contained bile, measured $\frac{1}{2}$ by $\frac{1}{4}$ inch and emptied readily on pressure. The fact that bile had entered the gall bladder and could be expressed from it without difficulty constituted fairly strong evidence against the presence of an obstructive lesion involving the extrahepatic biliary system, as had been suggested by the icterus and the presence of bile in the urine prior to operation.

The pancreas, which was quite mobile and could be visualized completely, measured about $\frac{3}{4}$ by $\frac{3}{16}$ inch. The spleen measured about $2\frac{1}{2}$ by $1\frac{1}{2}$ inches and was distinctly lobulated. The small bowel, commencing at the fossa of Treitz, was firmly contracted throughout its entire length, its diameter being about $\frac{3}{16}$ inch. The large intestine, which was completely hidden by the distended stomach except in the region of the hepatic flexure, also was contracted. It measured about 1 inch in diameter and contained a small amount of secretion in its distal portion. The appendix measured about $\frac{1}{2}$ by $\frac{1}{8}$ inch. No external, constricting peritoneal bands or folds or areas of atresia were noted involving the small or large bowel. The omentum, which was about 2 inches long, was extremely thin and delicate and of almost gelatinous consistency. It was light brown in color and appeared not having been encountered, attention was redirected to that point.

A short incision was made in the anterior wall of the juxtapyloric portion of the duodenum parallel to its long axis, and carried proximally to the pyloric ring. Bile-stained, duodenal secretion immediately flowed from the opening. This indication that the common bile duct was patent together with the evidence presented previously that the gall bladder contained bile and could be emptied on pressure constituted further, but not necessarily complete, proof of the absence of an anomaly of the biliary passages. (In the presence of icterus and bile in the urine, an obstruction in one of the branches of the hepatic duct still was theoretically compatible with the operative findings.) A large blunt probe was passed distally into the duodenum without encountering obstruction. It was then passed proximally through the pyloric ring for a short distance, where an impassable obstruction was met. Several attempts to overcome the obstruction being unsuccessful, the probe was withdrawn and pressure again was made on the proximal portion of the stomach in order to balloon up the antrum. As this was done and the edges of the duodenal incision were held open, a small nipplelike projection was seen to protrude through the pyloric valve and more globular. Its lumen of the duodenum for a short distance. As the stomach was still more firmly compressed, the nipplelike projection became distended and more globular. Its appearance now was that of a small balloon which, in part, had been forced from the gastric side of the pyloric ring into the lumen of the duodenum. It was grasped immediately with small forceps and incised with a scalpel. As this was done, gas and fluid escaped at once, and the stomach, the proximal portion of which was being compressed, collapsed. The short duodenal incision, which ended at the pyloric ring, then was continued proximally into the adjacent portion of the stomach for a distance of about $\frac{1}{2}$ inch and the lesion within the lumen exposed. It was found to consist of a complete septum or diaphragm, which lay transversely in the distal portion of the stomach, immediately proximal to the pyloric valve (Fig. 4a). Both surfaces of this diaphragm were covered by mucous membrane which merged at the periphery with the mucous membrane of the stomach and the adjacent pyloric valve. The edges of the stab wound previously made in the septum were grasped, and the latter was incised radially in several directions with the result that it retracted peripherally in every direction to such an extent that it was no longer distinguishable from the mucous membrane of the adjacent

If the pouch represented a dilated duodenum associated with a widely dilated, atonic pylorus, the thin barium mixture should have flowed back into the stomach fairly freely and, as a result of vomiting, the shadow under discussion should have become smaller or even disappeared. Instead, it grew larger and maintained its rounded contour. This sequence seemed to indicate the presence of strong muscular contraction in the area proximal to the barium-filled pouch. Since such muscular contraction is incompatible with a dilated, atonic pyloric sphincter, the diagnosis of duodenal dilatation seems unlikely. Even if it were assumed for the purpose of argument that the pouch represented a dilated duodenum separated from the stomach by a firmly contracted pyloric sphincter, the latter would have rendered it impossible for barium to have passed out of the stomach as quickly as it did in the first place. Accordingly, by a process of exclusion, it seems most logical to assume that the pouch represents the antral portion of the stomach separated from the body of the viscus by a contraction of the circular musculature (*musculus sphincter antri*) at the antral inlet. Schindler,¹² as the result of his gastroscopic observations, recently has drawn particular attention to this structure. A roentgen picture such as has been presented apparently is seen only in the earlier phases of pyloric obstruction when the antral (motor) portion of the stomach has undergone compensatory hypertrophy and moderate dilatation as the result of continued attempts to force the gastric contents beyond the point of obstruction. It is of interest to note that this was precisely the state of the antrum as disclosed at operation.

Although an anomalous obstruction, responsible for the major symptoms, was found in the prepyloric area, none was found in the biliary system to account for the icterus and bile in the urine, and none in the lower bowel to account for the failure of the child ever to pass meconium or to move its bowels prior to operation. The fact that the icterus subsided within a week of operation indicated that it was of the severe neonatal type, which, according to Holt and Howland,⁷ often occurs in association with premature birth. The passage of a small amount of meconium for the first time shortly after operation indicated that this symptom, as Alvarez¹ suggested, was due to the complete pyloric occlusion. The stimulus to intestinal peristalsis apparently originates primarily in the passage of gastric contents into the duodenum. Thus it may be assumed that normally a newborn child will pass meconium as soon as gastric secretion passes into the duodenum, even before food is taken. In our patient, since the obstruction in the prepyloric area was complete, no gastric contents passed into the duodenum and therefore the major stimulus was lacking. According to Ballantyne,³ amniotic fluid, vernix caseosa, lanugo hair, and epidermal cells normally are swallowed during fetal life and pass into the intestinal canal to increase the bulk of the meconium. It appears quite likely that the small amount of meconium noted in the colon at operation and passed by the child after operation was due to the failure of the above-mentioned constituents to pass from the stomach into the intestine during fetal life.

at the operative site. On the day after operation, a small amount of meconium and then stool were passed for the first time. The bowels thereafter moved several times daily. There was some elevation of temperature during the first two days, the peak being 101.8° . By the third day, temperature was normal. Two days after operation, x-ray films of the abdomen were made (Fig. 5). The stomach, which still was bilocular, was found considerably less distended than previously. The antral portion now was situated in front of the vertebral column instead of in the right side of the abdomen. Immediately beyond the antrum, the gas-filled first portion of the duodenum, resembling a reversed letter S, could be clearly visualized. Gas also was present for the first time in other portions of the bowel.

The feeding formula was increased rapidly in amount and was taken without vomiting. Jaundice began to subside and within a week practically disappeared. The wound healed kindly except for the occurrence of slight necrosis of the skin in the central portion. Alternate sutures were removed on the seventh day following operation and the remainder on the twelfth postoperative day. By that time the oral lesions (thrush), which had been treated by the local application of gentian violet, had subsided completely. Over a period of two and one-half weeks the child's weight increased from approximately 5 pounds to 6 pounds 3 ounces, and at the end of that time she was ready to be discharged from the hospital.

General Discussion.—At this point it is of interest to attempt to correlate the roentgenographic and clinical features of the case with the operative findings and postoperative course. In the light of the operative findings, which consisted primarily of a complete, transverse septum of mucous membrane in the prepyloric region, a reconsideration of the x-ray films is of value and may offer some criteria upon which the diagnosis of pyloric occlusion may be based in the future. Interest centers chiefly upon the distal air-filled pouch seen in Fig. 2 and the corresponding barium shadow in Fig. 3. In Fig. 1, although the stomach is diffusely distended, its contour is fairly normal. In Fig. 2 a bilocular organ is seen, the distal pouch being globular in shape and relatively more distended than the corresponding portion of the viscus in the preceding film. Whether this distal pouch represents the first portion of the duodenum or the pyloric antrum is uncertain. Another film (not reproduced in this article) was taken immediately after barium had been introduced into the stomach through a catheter. Under these circumstances, the distal air-filled pouch noted in Fig. 2 became filled with barium at once. This observation at first glance tended to support the view that the pouch represented the distal (antral) portion of the stomach. Another possibility, however, was that it represented the dilated, proximal portion of the duodenum. In order to render the second interpretation tenable, it was necessary to postulate that the pylorus was so atonic as to permit barium to flow from the stomach into the duodenum at once. (According to Morton and Jones¹⁰ and to Ladd,¹¹ such atony and dilatation of the pylorus occur quite regularly in association with marked duodenal dilatation above a point of obstruction.) After four hours, barium in increased amount had been forced into the distal pouch, while the remainder of the stomach contained practically none (Fig. 3).

partially lateral to the greater curvature of the stomach. These findings confirmed the diagnosis of obstruction of the small intestine. Because of the location of the distended loops, in the upper abdomen and chiefly toward the left side, the obstruction was considered to be situated in the jejunum. It was further assumed to have been produced by angulation or compression of the bowel by plastic exudate at or near the operative site.

Temperature had been normal during the twenty-four hours preceding the establishment of the diagnosis by roentgenography, and therefore it was assumed that the obstruction in all probability was not complicated by strangulation of the bowel. For that reason, it was decided to withhold operation, at least temporarily, and to await developments in the hope that spontaneous relief of obstruction would occur. One circumstance which militated against prolonged delay, however, was the increasing difficulty in administering fluids by parenteral routes.



Fig. 6.—Four months postoperatively. Upright film, ten minutes after ingestion of small amount of barium. Note normal antrum and first portion of duodenum. Barium already present in jejunum.

On the fifth day following the onset of symptoms, the temperature rose to 105° . By this time, fluids no longer could be administered intravenously since no patent veins could be found even by cutting down. At the same time, clyses were being absorbed poorly and the child was losing weight. Vomiting, obstipation, and abdominal distention continued, and, in view of the inability to overcome dehydration, the decision was made to operate. Accordingly, the child was taken to the operating room and, everything being in readiness for rapid exploration, drop-

An attempt to explain the presence of a complete septum of mucous membrane situated immediately proximal to the pyloric valve results in speculation. The first theory is that the septum is formed as the result of fusion of folds of mucous membrane which in this region normally are reduplicated to form the pyloric valve. A second explanation is that the septum represents an abnormally high occlusion of the duodenum, as suggested by Anders to explain the three cases of pyloric atresia reported by Hammer and by Sternberg. According to Tandler,¹² prior to the fifth week of gestation the intestine possesses a lumen lined with epithelium. Shortly thereafter the epithelium proliferates and fills the lumen to obliterate the latter completely. This solid stage lasts only a short time, to be followed by a stage in which multiple vacuoles appear. These vacuoles coalesce and by the twelfth week of fetal life the lumen normally is re-established. A failure of complete coalescence of the vacuoles results in the presence of residual areas of atresia or of septa which occlude the lumen, such occlusions being found most commonly in the duodenum. Accordingly, an abnormally high duodenal occlusion might possibly be considered the cause of the anomaly noted in the present case. Unfortunately a specimen of the mucous membrane forming the septum was not removed for microscopic examination, but there was no doubt that the septum was situated proximal to the pyloric ring.

Further Course.—On the eighteenth postoperative day, after sixteen days of normal temperature, there was a rise to 101.4° and the child vomited several times. Examination was negative except for the presence of a moderately severe pharyngitis, and it was assumed that the latter accounted for the fever and vomiting. On the following day, temperature rose to 106.2° and vomiting became more frequent. At that time the pharyngitis appeared more acute. By the third day temperature returned to normal, but vomiting continued and the bowels had failed to move for thirty-six hours. All feedings therefore were discontinued, and fluids again were given parenterally. Enemas at first resulted in the return of small amounts of stool, but subsequently were ineffectual even for gas. During the third day, the abdomen gradually became distended. In the presence of a clinical triad, consisting of persistent vomiting, obstipation, and increasing abdominal distention, the diagnosis of intestinal obstruction was made. The presence of bile in the vomitus and the abdominal distention contrasted with the clinical picture of the original obstruction in which both of these features were absent. Accordingly, it was postulated that the obstruction was not present at the original site, but at a point lower in the small intestine. An x-ray film of the abdomen taken on the fourth day of obstruction revealed the presence of a large fluid level which, because of its size and its position in the left upper quadrant, appeared to be situated within the stomach. Details of the abdominal viscera below the fluid level were obscured, however, by a diffuse haze which involved the entire abdomen. Within this hazy area a number of scattered fluid levels were seen, the largest being situated in the left half of the abdomen below the gastric fluid level mentioned previously. In order to establish the significance of these scattered levels more precisely, the stomach was emptied by tube, a tiny amount of barium introduced, and another film made. This revealed moderate gaseous distention of the stomach, the lower border of which was faintly demarcated by the barium, and disclosed the presence of several distended loops of small intestine containing gas and fluid. The most prominent of these were situated on the left side below and

5. Operation, performed on the fifth day of life, consisted of multiple incisions of the prepyloric septum and pyloroplasty. No other congenital anomalies were found.

6. The early postoperative course was uneventful. The icterus was concluded to be an accompaniment of prematurity. The failure to pass meconium was assumed to be due to a lack of the normal stimulus to intestinal peristalsis which apparently is initiated by the passage of gastric contents into the duodenum.

7. On the eighteenth postoperative day, the patient developed a secondary, complete intestinal obstruction. Five days later, as operation was about to be performed, the obstruction was relieved spontaneously. The course thereafter, although temporarily stormy, was one of improvement ending in recovery.

8. Follow-up x-ray studies, performed five months after operation, revealed the gastrointestinal tract to be normal except for the presence of rapid emptying of the stomach and intestinal hypermotility, apparently due to the pyloroplasty. The patient more than doubled her lowest weight during that period. The follow-up period now is seventeen months.

9. To the best of our knowledge, this case is the first of its kind to be reported. It also represents one of the very few successful attempts at major surgery upon a premature child and the earliest pyloroplasty. Finally, it appears to be the earliest case of postoperative intestinal obstruction recorded in the literature.

We express our appreciation to all who assisted in the care of the patient, and particularly to the members of the Attending Pediatric Staff and Pediatric House Staff, without whose valuable cooperation we doubt whether the child would have survived.

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ether anesthesia was begun. As the anesthetic was being administered, the child began to struggle violently and moved its bowels on the operating table. Anesthesia therefore was discontinued at once.

Feedings were begun within a few hours and were retained. The next day the bowels moved spontaneously and continued to do so regularly thereafter. During the next ten days, the child suffered an episode of severe stomatitis and pharyngitis associated with high irregular fever, which on one occasion reached 103° . At that time convulsions and Cheyne-Stokes respiration occurred but subsided under intensive treatment. Following this episode the course was one of improvement, the temperature slowly subsiding and the local pharyngeal manifestations clearing progressively. At the time of discharge from the hospital, five and one-half weeks after operation and two and one-half weeks after the spontaneous relief of the secondary intestinal obstruction, the wound was firmly healed, bowels were regular, the child was eating normally, and she had regained all of the weight previously lost. Thereafter she was observed regularly by one of us (R. M. S.).

At first the bowels moved four to five times daily, apparently as the result of rapid emptying of the stomach following pyloroplasty, but this symptom was controlled without difficulty by dietary regulation. A film, taken with the patient in the erect position ten minutes after the ingestion of a small amount of barium (Fig. 6), revealed the antrum and the first portion of the duodenum to be normal in size, shape, and position. A small amount of barium already was present in the jejunum. A film, taken in the prone position thirty minutes after the child began to ingest a full barium meal, revealed the stomach to be well filled. The antrum and the first, second, and third portions of the duodenum were clearly visualized and appeared normal. The head of the column of barium was in the region of the upper ileum, indicating rapid evacuation of the stomach and intestinal hypermotility as the result of pyloroplasty. Subsequent films revealed barium in the large intestine and close inspection failed to reveal the presence of any abnormality of the intestinal canal to indicate the site at which the postoperative intestinal obstruction previously had been present.

The child's present weight, approximately seventeen months after operation, is 30 pounds and she is entirely free of gastrointestinal symptoms. Although her mental and physical development have been normal, the facies strongly suggest the possibility of mongolism.

SUMMARY

1. Congenital obstructions of the stomach, exclusive of hypertrophic pyloric stenosis, are described and their extreme rarity discussed.
2. A unique case of congenital gastric obstruction, due to a complete prepyloric septum of mucous membrane, is described in detail. The patient was a premature infant.
3. Three and possibly all four offspring of the patient's father and the father's two sisters suffered from some congenital anomaly; exclusive of the patient, all died in infancy.
4. The presenting symptoms commenced at birth and were those of high obstruction. Additional clinical features were the failure of the child to pass meconium and the presence of icterus which was more intense than normal. These manifestations suggested the presence of additional obstructive anomalies, of the lower intestinal tract and biliary duct system respectively. X-ray examination indicated the presence of an obstructive lesion in the distal portion of the stomach or very first portion of the duodenum.

5. Operation, performed on the fifth day of life, consisted of multiple incisions of the prepyloric septum and pyloroplasty. No other congenital anomalies were found.

6. The early postoperative course was uneventful. The icterus was concluded to be an accompaniment of prematurity. The failure to pass meconium was assumed to be due to a lack of the normal stimulus to intestinal peristalsis which apparently is initiated by the passage of gastric contents into the duodenum.

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CEREBRAL HERNIATION THROUGH THE INCISURA TENTORII*

A CLINICAL, PATHOLOGICAL, AND EXPERIMENTAL STUDY

WILLIAM LISTER REID, M.B., M.Sc., MONTREAL, QUEBEC

(From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute)

THE openings which connect the anatomical subdivisions of the cranial cavity with each other and with the spinal canal frequently play an important role in the development of certain complications in cases of increased intracranial pressure. These openings are three in number: (1) the foramen magnum, (2) the opening beneath the falx, (3) the incisura tentorii. The boundaries of each are relatively rigid and nonyielding, and when the pressure in one compartment is increased, as by an expanding lesion, the contents tend to be forced through the connecting opening into the adjoining compartment. The signs that may be exhibited under these circumstances depend on the degree of pressure exerted by the herniated tissue on the neighboring structures.

The best known of the herniations occurs through the foramen magnum, particularly in expanding lesions of the posterior fossa. The opening beneath the falx, however, is probably the most frequent site for cerebral herniation and is usually the first opening through which it occurs in supratentorial expanding lesions. This can be seen by the midline shift in the x-ray films after oxygen has been injected into the ventricles.

In this report special consideration is given only to herniation through the incisura tentorii. This opening is triangular in shape (Fig. 1). Anteriorly it is limited by the basilar portion of the occipital bone, and laterally by the rigid free borders of the tentorium cerebelli. On each side immediately above the tentorial edge lies the hippocampal gyrus in such a position that, when pressure is exerted from one of the hemispheres, this structure is the one that is forced over the edge. Within the confines of the incisura, and in close relationship to the hippocampal gyrus, lie the third nerves, the cerebral peduncles, the midbrain, and the posterior cerebral arteries and their branches (Fig. 2). As the free space in the incisura is very limited, it is easily understood how any herniation from above may press on the underlying structures or interfere with the flow of blood through the vessels and produce one or more of the clinical symptoms or pathological changes

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to be described. Herniation through the incisura tentorii is a common occurrence as a late complication in expanding supratentorial lesions. It is my aim to demonstrate the pathological lesions which the herniations cause and describe the clinical signs that such patients may show. For the purpose of this study the records of 32 patients with supratentorial expanding lesions showing the clinical signs or pathological changes to be described have been studied. Twenty-five of these were examined at necropsy. A variety of supratentorial expanding lesions are included in the series. There were 21 cases with neoplasms, 6 extradural and 2 subdural hemorrhages, 2 intracerebral abscesses and



Fig. 1.—Photograph of base of normal skull with part of right temporal and occipital lobes left in place. H, hippocampal gyrus; N, third nerve nucleus; MB, mid-tentorium cerebelli; T₁, free edge of tentorium cerebelli; T₂, attached edge of tentorium cerebelli; J, third nerve.

1 tuberculoma. The results from a group of 10 successful experiments in which supratentorial expanding lesions were produced in 10 macacus rhesus monkeys are included. In each of the 25 cases that were examined at necropsy, and in each of the experimental animals there was a herniation over the free edge of the tentorium cerebelli and histologically this herniation always revealed the structure of a distorted, sometimes strangulated, hippocampal gyrus (Fig. 3). In the more marked cases this herniation was projected downward in the form of

a wedge between the tentorial edge and the midbrain. In most instances the herniation was marked, but in some, often contrary to expectation, it was only slight. In the latter cases it was assumed that after death the herniated tissue had shrunk and largely returned to its normal position. The degree of herniation found in the animals was usually much greater than in the clinical cases, because the animal brains were always hardened in situ with formalin to prevent any recession of the herniation. In general, in both clinical and experi-



Fig. 2.—Photograph of base of brain showing the relationship between the herniated hippocampal gyrus, the third nerve, the blood vessels, and the midbrain. *H*, Herniated hippocampal gyrus; *PC*, posterior cerebral artery; *SC*, superior cerebellar artery; *G*, groove in herniated tissue made by the third nerve; *X*, groove made by free edge of tentorium cerebelli; 2, optic nerve; 3, oculomotor nerve.



Fig. 3.—Section through the herniation stained with thionin, showing that the herniated tissue has the same structure as the hippocampal gyrus. *H*₁, Hippocampal gyrus; *H*₂, herniated tissue. The arrows indicate the position of the tentorium cerebelli.

mental cases, the degree of herniation was roughly proportional to the amount of displacement produced by the primary expanding lesion.

In 17 of the 25 cases that came to necropsy, there was one or more of the following clinical signs present which it seems clear were due to the herniation: (1) ipsilateral third nerve palsy, partial or complete; (2) ipsilateral hemiplegia; (3) evidence of midbrain involvement and, from the pathological standpoint, in addition to the herniation: (a) infarction of one or more occipital lobes; (b) hemorrhages into the midbrain and pons; (c) partial occlusion of the cerebral aqueduct. In the other 8 necropsy cases these features were not observed although there were varying degrees of herniation present. This shows that the herniation may exist without causing any of the above clinical signs and without producing secondary damage to adjacent structures.

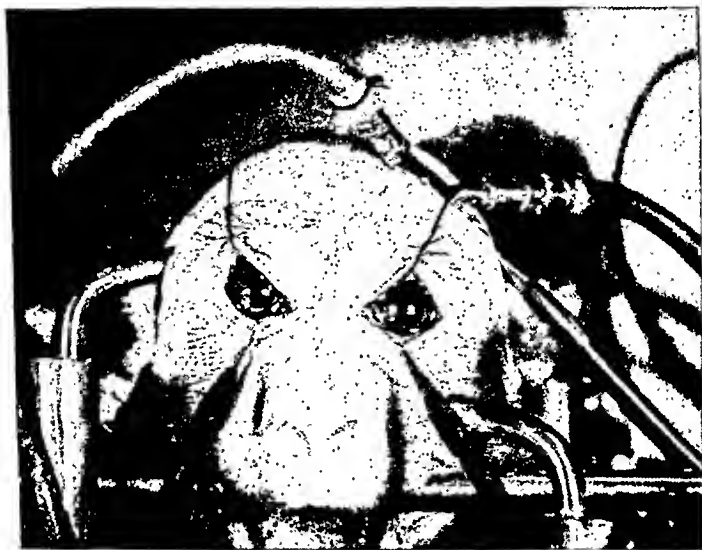


Fig. 4.—Showing the apparatus used in the acute experiments and the fixed dilatation of the ipsilateral pupil.

In the experimental animals an attempt was made to reproduce the signs found in human beings by means of an artificial extradural expanding lesion. Under general anesthesia a burr hole was made through the skull, the exact location varying slightly in each animal, but most often situated in the anterior two-thirds of the head. In the acute experiments (Fig. 4), after stripping the dura for a short distance around the burr hole, a Forbes window was screwed into the bone. One outlet was closed off and the other led by a rubber tubing to a large bottle of Ringer's solution. This was connected to a Woulfe bottle, which in turn was connected to the air pressure tap, and a mercury manometer. The fourth outlet from the Woulfe bottle was used as a safety valve. In this manner it was possible to force Ringer's solution into the extradural space at any desired pressure. It was

found that the best pressure to produce the desired results was 90 to 110 mm. of mercury. If greater pressure was used, the animal became deeply comatose and stopped breathing, and would die if the pressure were not released for a few minutes.

In the more prolonged experiments moistened saraka seeds or tragacanth was packed into the extradural space and the burr hole closed by means of a metal screw. The animal was then allowed to recover from the anesthetic and was carefully watched until it died. After death the arterial and venous systems were washed clean with Ringer's solution, and then irrigated with 10 per cent formalin to fix the brain in situ before it was removed. The acute experiments lasted from four to eight hours, while the time for the more prolonged experiments varied from twenty-five hours to four days. The complications resulting from herniation of the hippocampal gyrus over the free edge of the tentorium cerebelli are considered under two headings, first, the clinical signs which it may produce, and second, the pathological alterations it may cause.

CLINICAL SYMPTOMS

Ipsilateral Third Nerve Palsy.—The third nerve carries fibers that supply three separate groups of muscles: (1) the pupilloconstrictor muscle of the iris; (2) the levator palpebrae; (3) the rectus superior, rectus inferior, rectus internus, and obliquus inferior. There is fairly strong evidence to show that the fibers to the iris are separate and distinct from those supplying the other two groups. Hoessly (1918)¹ stated that "the iris fibers were more sensitive than those supplying the extraocular muscles, for they may show paresis without any affection of the extraocular muscles." In our clinical cases and animal experiments this was borne out. In each case in which the changes were closely observed throughout the various stages the pupil first began to dilate and soon lost its reaction to light. This was closely followed by ptosis of the upper lid and then by limitation of inward rotation of the eyeball. In Case 1 this series of events was well demonstrated.

CASE 1.—*Neoplasm of right parietal region. Ipsilateral third nerve palsy.*

A. C., male, aged 10 years. This child was admitted to the hospital complaining of headache, vomiting, drowsiness, and left-sided weakness. He had had transient periods of unconsciousness during which there was generalized rigidity. A biopsy from the right parietal region disclosed a rapidly growing glioma and no further operative interference was considered to be warranted. Before his discharge from the hospital there were three opportunities to observe the attacks of unconsciousness and rigidity inadequately described by the parents as they had seen them at home. In each one of the three episodes the course of events was identical. Generalized rigidity made its appearance and consciousness was rapidly lost. The ipsilateral pupil began to dilate slowly and soon lost its reaction to light. Before the pupil became fully dilated, the upper lid began to droop and it was

then noted that the eye turned out. Though the unconsciousness and rigidity lasted but two minutes, it took about five minutes for the paralytic third nerve signs to disappear.

The patient was discharged from the hospital and, when he died at home, the referring physician was unable to arrange for a post-mortem examination.

In the animal experiments this order of events was reproduced. Case 1 also serves to emphasize the importance of careful and repeated observation of the pupils, for, if they had not been closely watched, the third nerve changes might well have been missed.

It must not be taken for granted that pupillary changes always indicate an intracranial lesion. A dilated pupil, with or without fixation to light, may be due to one of many causes. Although Brooks (1921)² believed that unequal pupils were always pathological, Barrie (1918),³ after examining the eyes of 326 men, found that approximately 10 per cent of them had unequal pupils without any other signs of disease of the eyes or central nervous system.

Local eye disease, such as blindness, glaucoma, optic atrophy, etc., may cause unequal pupils, and certain drugs, such as atropine, homatropine, cocaine, etc., if introduced into the eye, will produce a dilated and fixed pupil. MacDonald (1921)⁴ described such a case in which belladonna was accidentally introduced into the eye with a resulting dilated and fixed pupil.

An excitatory lesion in the path of the cervical sympathetic must be considered. Hopkins (1925)⁵ observed that unilateral dilatation and fixation of the pupil were sometimes seen in cases of pulmonary tuberculosis, and he assumed that it was due to stimulation of the sympathetic chain by the pressure of the enlarged bronchial glands. He also cited a case in which the pupils were slightly unequal in a patient with syphilis. So it is clear that all extrinsic causes of pupillary changes must be eliminated before assuming that the lesion lies within the cranial cavity.

A detailed account of the evidence that was accumulated with regard to third nerve palsy has already been reported by Reid and Cone.⁶ Their conclusions were that ipsilateral third nerve palsy, partial or complete, occurring in cases of intracranial expanding lesions, was due to direct pressure on the third nerve by a herniation of the hippocampal gyrus over the free edge of the tentorium cerebelli. This is well demonstrated in Fig. 2 where the third nerve is flattened and has formed a groove in the herniated tissue.

In some of the clinical and experimental cases that have been studied with regard to this feature, one or more of the other five features were also present, but in each case the signs of third nerve palsy were observed first. In other words, when herniation of the hippocampal gyrus occurs, the ipsilateral third nerve, being the closest structure, is the first to feel the effects of pressure exerted by the herniated tissue. As the herniation increases, it may press on one or more of the

other structures in the incisura with the production of signs depending on the structure that is involved.

Ipsilateral Hemiplegia.—Not infrequently cases are seen in which there is an ipsilateral hemiparesis or hemiplegia associated with an intracranial expanding lesion. This may be confusing as a localizing sign, and it has often led to an exploratory operation on the wrong side. With modern methods of visualizing the ventricular system the possibilities of such an error have been greatly diminished. Even now, however, in certain cases of head injury the surgeon usually makes a burr hole on each side of the skull, partly to avoid the chance of an error in localization and partly because of the possibility of a bilateral hemorrhage.

Purves-Stewart (1927),⁷ Flateau (1924),⁸ Putnam and Cushing (1925),⁹ Groenvelde and Schaltenbrand (1927),¹⁰ Woltman (1928),¹¹ and others have reported such cases of ipsilateral hemiplegia. In each of the seven cases described by Rand (1929)¹² in relation to ipsilateral dilatation of the pupil in cases of intracranial hemorrhage, there was also ipsilateral hemiplegia. Kernohan and Woltman (1929)¹³ published a very concise report of 42 cases of intracranial expanding lesions, 37 of which were supratentorial. The reason for this report was to explain the mechanism by which ipsilateral hemiplegia was produced in such cases. Their conclusion was that it was caused by compression of the opposite crus cerebri against the sharp rigid free edge of the tentorium cerebelli, producing a notch in the crus and destruction of the tissue at the point of contact. They also observed that there may be herniation through the incisura tentorii as evidenced by the groove along the uncinate gyrus on the side of the primary expanding lesion. Twenty-two of their cases showed ipsilateral hemiplegia and notching of the crus; 2 showed mild ipsilateral signs without any notching; and the remaining 18 showed notching of the opposite crus but no signs of hemiplegia.

Hoen (1935)¹⁴ described 3 cases of cerebral expanding lesions with signs of ipsilateral weakness or paralysis. He, too, believed that it was due to the pressure of the lesion pushing the brain toward the opposite side and compressing the midbrain against the tentorial edge. He felt that the syndrome produced was diagnostic of a lesion in the frontoparietal region.

In our own experimental studies 2 of the animals developed ipsilateral hemiplegia. In each case this was preceded by ipsilateral fixed dilatation of the pupil and ptosis of the upper lid. At necropsy marked herniation of the hippocampal gyrus over the free edge of the tentorium was found, but there was no notching of the crus, nor were any pathological changes found in the midbrain microscopically. In only 1 of the 32 clinical cases (Case 2) was there ipsilateral hemiplegia.

CASE 2.—Large extradural hematoma left temporoparieto-occipital region. Ipsilateral third nerve palsy, hemiplegia, and occipital lobe infarction.

S. W., male, aged 30 years. This patient was unconscious for some time following a head injury. After a lucid interval of an hour or so he again became uncon-

scious and the attending physician noted a dilated and fixed pupil and hemiplegia on the left side. On admission to hospital he was in deep coma and both pupils were dilated and fixed.

At operation a large hematoma was found on the left side extending from the temporal region well back over the occipital lobe. Although the brain returned to its normal position and was pulsating well after the removal of the clot, the patient's condition did not improve and he died four days later.

At necropsy the following points were noted: (1) herniation of the left hippocampal gyrus over the tentorial edge; (2) slight indentation of the right crus cerebri with hemorrhagic softening of its substance (Figs. 5 and 6); (3) large area of infarction in the left occipital lobe and a small one in the right.

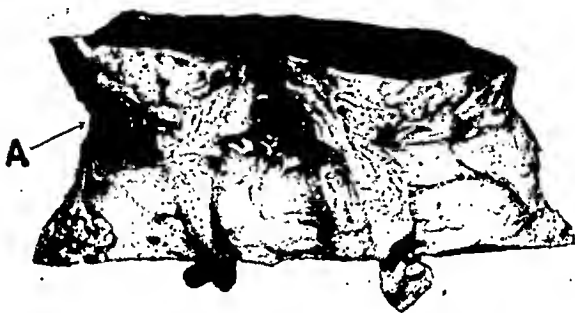


Fig. 5.—Showing notch in right crus cerebri made by the tentorial edge; A, notch.



Fig. 6.—Showing hemorrhagic softening of the right crus cerebri. A, Right crus; B, infarction in left temporal and occipital lobes.

From the work of Kernohan and Woltman the mechanism involved in this feature is quite clear. As they have shown, if the primary lesion is large enough it pushes the brain toward the opposite side and forces the opposite crus against the sharp free edge of the tentorium, causing

other structures in the incisura with the production of signs depending on the structure that is involved.

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Purves-Stewart (1927),⁷ Flatau (1924),⁸ Putnam and Cushing (1925),⁹ Groenvelt and Schaltenbrand (1927),¹⁰ Woltman (1928),¹¹ and others have reported such cases of ipsilateral hemiplegia. In each of the seven cases described by Rand (1929)¹² in relation to ipsilateral dilatation of the pupil in cases of intracranial hemorrhage, there was also ipsilateral hemiplegia. Kernohan and Woltman (1929)¹³ published a very concise report of 42 cases of intracranial expanding lesions, 37 of which were supratentorial. The reason for this report was to explain the mechanism by which ipsilateral hemiplegia was produced in such cases. Their conclusion was that it was caused by compression of the opposite crus cerebri against the sharp rigid free edge of the tentorium cerebelli, producing a notch in the crus and destruction of the tissue at the point of contact. They also observed that there may be herniation through the incisura tentorii as evidenced by the groove along the uncinate gyrus on the side of the primary expanding lesion. Twenty-two of their cases showed ipsilateral hemiplegia and notching of the crus; 2 showed mild ipsilateral signs without any notching; and the remaining 18 showed notching of the opposite crus but no signs of hemiplegia.

Hoen (1935)¹⁴ described 3 cases of cerebral expanding lesions with signs of ipsilateral weakness or paralysis. He, too, believed that it was due to the pressure of the lesion pushing the brain toward the opposite side and compressing the midbrain against the tentorial edge. He felt that the syndrome produced was diagnostic of a lesion in the frontoparietal region.

In our own experimental studies 2 of the animals developed ipsilateral hemiplegia. In each case this was preceded by ipsilateral fixed dilatation of the pupil and ptosis of the upper lid. At necropsy marked herniation of the hippocampal gyrus over the free edge of the tentorium was found, but there was no notching of the crus, nor were any pathological changes found in the midbrain microscopically. In only 1 of the 32 clinical cases (Case 2) was there ipsilateral hemiplegia.

CASE 2.—*Large extradural hematoma left temporoparieto-occipital region. Ipsilateral third nerve palsy, hemiplegia, and occipital lobe infarction.*

S. W., male, aged 30 years. This patient was unconscious for some time following a head injury. After a lucid interval of an hour or so he again became uncon-

necropsy, in each case, there was seen marked herniation of the hippocampal gyrus forming a wedge between the free edge of the tentorium and the midbrain (Fig. 7). A similar series of events was seen in Case 3.

CASE 3.—Large intracerebral neoplasm in right temporoparietal region.

W. S., male, aged 45 years. Prior to operation a ventriculogram was done and the patient placed on the x-ray table. While the pictures were being taken, he suddenly became rigid and stopped breathing and it was noted that the ipsilateral pupil had become dilated and fixed to light. A brain needle was immediately inserted into the ventricle and some fluid and gas escaped under fairly high pressure. The patient recovered rapidly to his original condition and the pupils returned to normal more slowly.



Fig. 7.—Experimental animal with extradural hygroma, showing herniation of the hippocampal gyrus forming a wedge between tentorium and midbrain and compression of the latter. Also showing narrowing of cerebral aqueduct. *H*, Herniated hippocampal gyrus; *X*, groove made by the sharp tentorial edge.

When considering the mechanism of pressure on the midbrain in cases of supratentorial expanding lesions, it is clear that the herniated hippocampal gyrus is of the utmost importance and it may be necessary to treat the herniation as well as the primary expanding lesion. Jefferson (1938)¹⁵ reported one case with a right temporal lobe neoplasm and an ipsilateral dilated and fixed pupil. He removed the entire temporal lobe together with the herniated tissue and the patient made a complete recovery. Vincent, David and Thiébault (1936)¹⁶ stated that they had removed the herniated tissue in certain cases and that the patients had recovered. In two of my own cases the herniations were not relieved by the removal of the extradural hematomas which had produced them and the patients died. It seemed from the post-mortem examinations that the herniations must have receded somewhat after the removal of the primary lesion but that the pressure on the midbrain was not completely relieved. Therefore, in agreement with Jefferson, it is suggested that the surgical procedure must also include

an interference with the conduction of nerve impulses and resulting in weakness or paralysis on the ipsilateral side. In addition to this I wish to emphasize the relationship that exists between the hemiplegia and the herniation of the hippocampal gyrus. It is my belief that, when the pressure exerted by the primary expanding lesion is sufficient to force the midbrain against the opposite tentorial edge, herniation of the hippocampal gyrus is invariably present. I also feel that the herniation is important in providing an additional and more direct line of force in pushing the midbrain against the opposite tentorial edge.

Signs of Midbrain Involvement.—One often sees a patient with a supratentorial expanding lesion admitted to the hospital with signs of midbrain involvement, such as deep coma, spasms of rigidity like those of a decerebrate animal and set off by the slightest stimulus, hyperpnea, tachycardia, and hyperthermia. These symptoms may be due to the pressure of the herniated hippocampal gyrus on the midbrain or to hemorrhage into the midbrain as will be pointed out later on.

When the pressure of the primary expanding lesion is great enough to force the hippocampal gyrus downward over the tentorial edge and through the incisura tentorii, the herniated tissue acts as a wedge inserting itself between the free edge of the tentorium laterally and the midbrain medially. The midbrain is thus compressed between the herniated tissue on the one side and the opposite tentorial edge on the other. The effects of the pressure exerted by these two structures differ in many respects. As the midbrain is forced against the sharp rigid tentorial edge, the damage that is done is mostly confined to the point of contact which, in this case, is the crus cerebri. As has been shown by Kernohan and Woltman, this results in an ipsilateral weakness or paralysis. On the other hand, the herniated tissue is broader, softer, and more pliable, so that the effect of its pressure is spread more evenly throughout the midbrain. The latter pressure is probably the main factor in the production of the signs of coma, decerebrate rigidity, etc., signs that indicate a near terminal or terminal stage in these cases.

Further evidence in this regard was obtained from two of the experimental animals. In each case fluid pressure was used forming an extradural hygroma which was connected to the air pressure tap and a mercury manometer. When the pressure was raised rapidly to 110 mm. of mercury, each animal became unconscious, the ipsilateral pupil dilated and soon lost its reaction to light, the upper eyelid dropped, and inward rotation of the eyeball was lost. There was marked spasm resembling that seen in decerebrate rigidity; respiration became labored and then ceased, and the heart beat stopped. All this took place in about ten seconds. On release of the pressure the animals rapidly recovered. This procedure was repeated several times in each animal with the same result. Finally, the pressure was maintained at 110 mm. of mercury until the animals died and the brain was then fixed in situ. At

In our animal experiments the extradural pressure necessary to produce even marked herniation was always less than the systolic blood pressure. The pressure at the point of the herniation would be less still, and probably much less than would be necessary to compress the artery directly. It is possible that, once the herniated wedge is in position, the addition of edema in the herniated tissue may supply the additional pressure necessary to compress the vessel, but, if this were the case, one would expect occipital lobe infarction to be much more common.

The points that we wish to emphasize in relation to occipital lobe infarction occurring in cases of supratentorial expanding lesions are: first, the constant presence of herniation of the hippocampal gyrus over the free edge of the tentorium; second, that this herniation is an essential part of the mechanism involved in the production of the infarction; and, third, the constant association of ipsilateral third nerve palsy in each of these cases.

Hemorrhage Into the Midbrain and Pons.—It is not at all uncommon, on sectioning the brains of patients who have died from an intracranial expanding lesion, to find hemorrhages in the midbrain and pons. These hemorrhages vary considerably in size. Some consist merely of a diapedesis of blood cells around the vessels, while in others there may be massive hemorrhages with considerable destruction of the surrounding tissue. Moore and Stern reported eleven such cases and they believed that the herniated hippocampal gyrus was an essential part of the process involved. Our own studies have helped to confirm this viewpoint, but the evidence that we have obtained has not been sufficient to enable us to formulate any theory as to the exact manner in which the herniation produces the hemorrhage.

In 9 of the 25 brains of this group that were examined at necropsy, there were midbrain and pontine hemorrhages. In 7 of these 9 cases signs of third nerve palsy were observed before death and in 1 of this group there was bilateral occipital lobe infarction. Also in all 9 cases there was herniation of the ipsilateral gyrus over the free edge of the tentorium. Observations add nothing to and only confirm the findings of Moore and Stern as far as the midbrain hemorrhages are concerned, but I do want to emphasize that, when herniation caused midbrain and pontine hemorrhage, the presence of the herniation was at least suggested before death in 7 of the 9 cases by the ipsilateral third nerve palsy.

Obstruction of the Aqueduct of Sylvius.—In many of the cases examined at necropsy the cerebral aqueduct has been so greatly distorted and displaced by the herniation that it would seem to have been functionally blocked. This feature has been more clearly demonstrated in some of the experimental animals where the brains were fixed in situ by intravascular injection before removal. In Fig. 7 the aqueduct is seen to be narrowed. In another monkey (Fig. 8) it was almost completely occluded.

either manipulations to prove the hernia is reduced or removal of the herniated tissue if reduction is not complete. It may in some instances be advisable to enlarge the opening by incision of the free edge of the tentorium. The fact that in some of our recovered cases this was not done shows the herniation may correct itself, but it is leaving less to chance if the region is at least inspected, the necessary retraction for exposure of the area being itself of value to reduce a small hernia after the primary cause of the intracranial pressure increase has been corrected.

PATHOLOGICAL CHANGES

Infarction of One or Both Occipital Lobes.—This is a comparatively rare complication but one that comes within the scope of this study. Meyer (1920),¹⁷ in discussing herniation of the brain, described several cases of supratentorial expanding lesions that showed a "tentorial line" along the uncus where it had herniated over the edge of the tentorium cerebelli. In one of these cases the blood flow through the right posterior cerebral artery was interfered with by the herniation, and this resulted in collapse of the corresponding part of the occipital cortex. Another case in the same series revealed a much larger herniation, but there was no evidence of interference with the blood flow. Moore and Stern (1938)¹⁸ described five cases in each of which there was occipital lobe infarction associated with an intracranial expanding lesion. They felt that the infarctions were due to compression of the posterior cerebral artery.

In four of my own series of cases there was occipital lobe infarction. In each case there was a unilateral intracranial expanding lesion which was associated with ipsilateral fixed dilatation of the pupil and herniation of the hippocampal gyrus over the free edge of the tentorium cerebelli. In three of these cases the occipital lobe infarction was bilateral but more marked on the ipsilateral side. In each of these 3 cases there was bilateral herniation of the hippocampal gyrus, but also more marked on the side of the primary expanding lesion. In the fourth case the infarction was unilateral and on the same side as the expanding lesion, as also were the herniation and the third nerve palsy.

At necropsy we were unable to make out the exact mechanism involved in interfering with the blood supply to the occipital lobes, but it was evident that the herniated hippocampal gyrus was an essential part of that mechanism. Because of the rarity of this condition as compared with the frequent occurrence of the herniation, and the fact, as seen in Meyer's two cases, that infarction is not necessarily dependent on the size of the herniation, we feel that the interference with the blood supply to the occipital lobes is probably due to some anomaly in the anatomical course of the vessels. In this manner the arterial obstruction is due to stretching or kinking of the vessel by the herniation rather than to direct compression.

conclusive proof that the lumbar and ventricular pressures are not of necessity always equal." I concur in this, but, when they add, "a difference was observed only in cases where the lumbar pressure was abnormally high," and then go on to say, "it seems therefore that a normal lumbar puncture pressure in a case of intracranial tumor is a true index of the intracranial pressure," I take issue. While it holds in the cases they studied, it seems to me to be unwarranted as a general conclusion as the following case suggests.

CASE 4.—B. O., female, aged 25 years, had suffered right frontal head injury one-half hour before admission to the hospital. She had recovered consciousness after a few minutes and then was nauseated and her senses became dull. The left abdominal reflexes were absent and the left biceps and knee jerk were slightly accentuated. The pulse was 100 and the blood pressure was 128/72. The spinal pressure was 120 mm. of water and the spinal fluid was bloody. Following the lumbar puncture her senses became more dulled; left-sided weakness with accentuated deep reflexes developed. The pulse fell to 76 and then to 66. A second lumbar puncture was done and the pressure was 60. The right pupil dilated and became fixed to light; respirations became stertorous and the patient became deeply comatose. Following hypertonic glucose the general condition improved slightly. Lumbar puncture then showed the pressure to be too low to record. Because of the low spinal pressures it at first was decided that an extradural hemorrhage could not be present and that the symptoms were due to advancing hemorrhages in the midbrain. As the patient's condition became worse a subtemporal exploration was carried out four hours after the accident in spite of the low spinal pressure because the course of events was so typical of extradural hemorrhage. An extradural clot and fluid blood with an estimated volume of 300 c.c. was present, producing much pressure and much deformity. The bleeding point from the middle meningeal artery was easily secured. The brain expanded but little after the clot was removed. She died two days later never having recovered consciousness.

It was the 1931 notes of this catastrophe that led us to study extradural compression experimentally and led on to an investigation of the temporal pressure cone. The case illustrated the point not only that lumbar puncture in such cases may be followed by a marked progression of signs but that lumbar pressures may give no true index of the intracranial pressure.

SUMMARY

As supratentorial intracranial expanding lesions increase in size, pathological alterations may take place at a distance from the primary lesion due to brain shift and herniation into adjacent intracranial compartments. The extent of the herniation and shift depends on the force exerted by the primary lesion and the clinical signs depend on the structures encroached on by the displaced brain.

Herniation of the hippocampal gyrus of the temporal lobe through the incisura of the tentorium cerebelli is a common occurrence in supratentorial space-occupying lesions. Clinically it can cause ipsilateral third nerve paresis or paralysis, ipsilateral hemiplegia, signs of midbrain involvement, and obstruction to the aqueduct of Sylvius. Grave irreversible damage to important structures may be produced

We have only cursory clinical evidence to show that the aqueduct may be obstructed by herniation since it has not been our custom to take simultaneous ventricular and lumbar pressures. The work of Smyth and Henderson¹⁹ proves the point conclusively. Eight of 33 tumor cases which they studied showed a disturbance of dynamics. Six of these had supratentorial tumors and they had an initial pressure difference, the ventricular readings being from 20 to 100 mm. of water higher than the spinal ones. This disparity was accentuated by the withdrawal of lumbar fluid. In these 6 cases jugular compression also proved a partial block. When the ventricular pressure was higher than

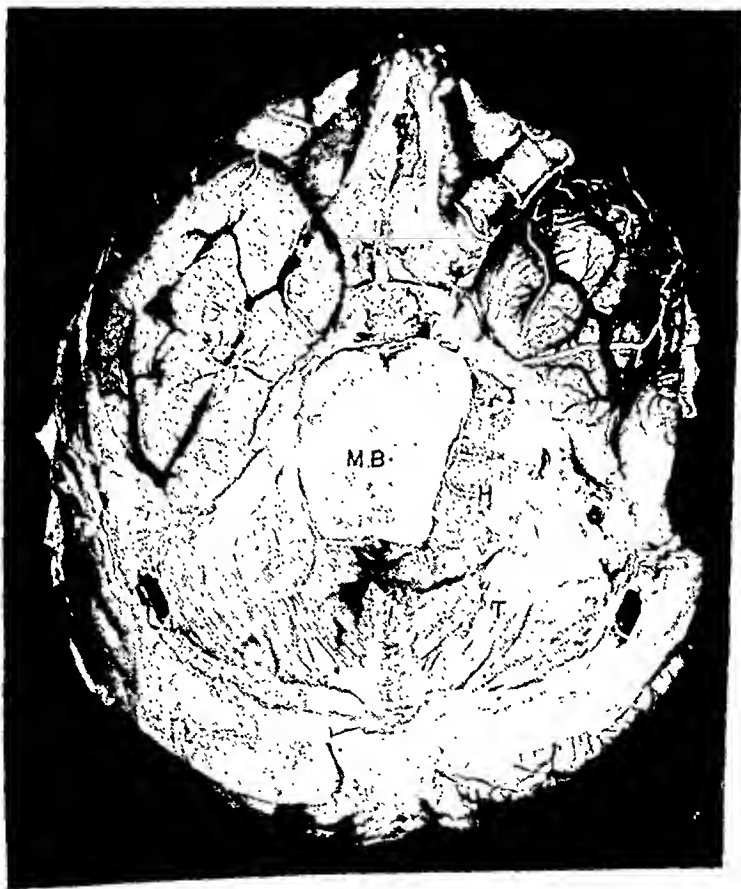


Fig. 8.—Showing a large herniation of the hippocampal gyrus with compression of the midbrain and almost complete occlusion of the cerebral aqueduct. MB, Midbrain; H, herniation.

the lumbar pressure there was a high operative mortality. The six patients died and post-mortem evidence of herniation of the temporal lobe through the incisura tentorii was found.

I question only one of the statements in their discussion, though the points in my experience leading me to query it are not beyond criticism. They state: "It is apparent that the observations here recorded afford

CEREBELLAR SUBDURAL HEMATOMA IN INFANT 2 WEEKS OLD WITH SECONDARY HYDROCEPHALUS

OPERATION WITH RECOVERY

RICHARD G. COBLENTZ, M.D., BALTIMORE, MD.

(From the Departments of Pathology and Neurosurgery, University of Maryland Medical School)

THE formation of a subdural hematoma following intracranial hemorrhage in the newborn probably occurs more frequently than is generally recognized. In fact, Ingraham and Heyl¹ in a recent article state that "it is a common condition in infancy and early childhood" and that "the frequency with which subdural hematoma is found among children is more or less proportional to the intensity with which it is sought." This statement is, perhaps, particularly true in young infants, in whom a subdural clot is more apt to be accompanied by subarachnoid bleeding which may mask the presence of the subdural lesion. Failure to recognize either of the two types of hemorrhage, if the infant survives for any length of time, frequently results in the development of a secondary hydrocephalus due to (1) interference with the absorption of the cerebrospinal fluid or (2) the mechanical obstruction to flow of the cerebrospinal fluid from the ventricular system.

It is a well-recognized fact that trauma is, perhaps, the most frequent cause of subdural hematoma in adults, but that systemic diseases, especially those affecting the vascular system of the brain, may play an important secondary role. In infants and children trauma is considered an important etiologic factor by Ingraham and Heyl.¹ Other investigators (Sherwood,² Peet and Kahn,³ Rosenberg,⁴ and Ingalls⁵) call attention to the fact that subdural hematoma occurs frequently in undernourished infants, infants with scurvy and other dietary deficiencies, and particularly in those with vitamin C deficiency in which no history or evidence of trauma can be obtained.

As in adults, the location of the subdural hematoma in infants is almost invariably over one or both of the cerebral hemispheres. Very rarely does an encysted subdural clot form in the posterior fossa over the cerebellar hemispheres, either in adults or infants. Dandy⁶ has reported a case in which an encysted clot was found in the pituitary region, producing symptoms of a pituitary tumor. The lesion was found at operation and the patient recovered after evacuation of the clot. Putnam and Cushing⁷ cite a case of Naffziger⁸ in which the hematoma was chiefly basal in the region about the mastoid, fading out toward the vault. This patient also recovered after operation. The lesion involved the spinal cord also in several cases in the literature.⁹

by it, such as infarction of the occipital lobes and pontine hemorrhages, damage to the crura cerebri and hemorrhage and softening of the herniated gyrus.

As has been shown in a previous report, one of the earliest signs of incisural herniation that will cause damage is dilatation of the ipsilateral pupil. Dilatation of the ipsilateral pupil has commonly occurred in this series of patients before ipsilateral paralysis of the extremities and the other signs of graver damage. It is important to recognize and evaluate properly the significance of the secondary clinical signs that occur as a result of these herniations and realize the pathological alterations that result from them if prompt treatment is not instituted. The herniation of the hippocampal gyrus may not recede after the primary expanding lesion is removed and the surgeon must keep this possibility in mind, for Jefferson and others have removed the strangulated gyrus after treating the primary lesion with recovery of the patient.

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COBLENTZ: CEREBELLAR SUBDURAL HEMATOMA IN INFANT 2 WEEKS OLD WITH SECONDARY HYDROCEPHALUS

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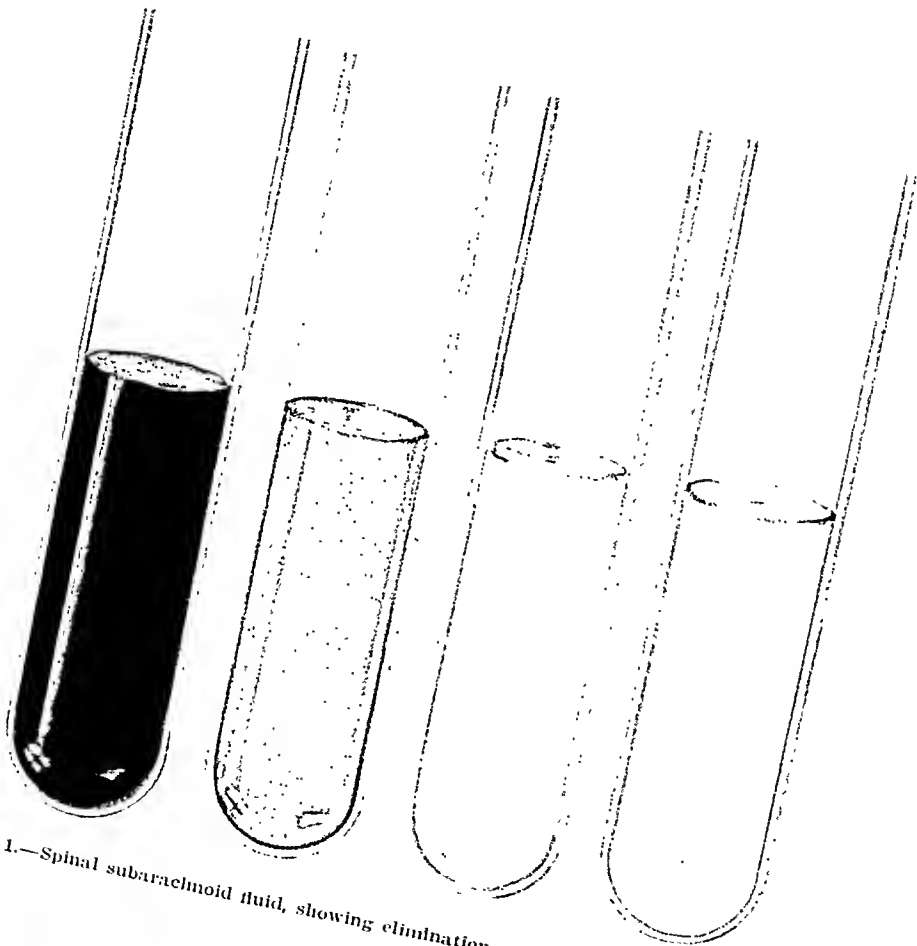


Fig. 1.—Spinal subarachnoid fluid, showing elimination of blood by spinal drainage.

In a fairly extensive review of the literature only four cases of encysted subdural hematoma in the posterior fossa over the cerebellum were reported. All these cases were found at autopsy and had not been recognized before death. Neisser and Pollack¹⁰ mentioned two cases found at autopsy, cited by Putnam and Cushing.⁷ Pieken¹¹ reported one case found at autopsy, no operation, included in a report of a series of cases by Jelsma.¹² The fourth case, reported by Munro,¹³ was a right subdural hematoma, together with a cerebellar subdural hematoma. Death occurred eleven days after evacuation of a right cerebral clot, with the discovery of bilateral cerebellar hematoma at autopsy. In no instance was there a record of an encysted subdural hematoma over the cerebellum which had been recognized and cured by operation.

The chief object of this paper is to record a single case of encysted subdural hematoma over the right cerebellar hemisphere, with secondary hydrocephalus, in an infant 2 weeks old, verified at operation, with recovery.

CASE REPORT

Baby K., aged 9 days, was transferred to the Neurosurgical Service from the Obstetrical Department of the University Hospital on Oct. 24, 1939, because of enlargement of the head and bulging fontanelles, with marked separation of the cranial sutures.

The note on the obstetrical chart was as follows: "Mother admitted from the Out-Patient Department on Oct. 15, 1939, at term and in active labor. Multipara ii. Normal deliveries. Prenatal course with this pregnancy uneventful. Labor progressed normally under routine nembutal and paraldehyde analgesia, and after two hours and forty-three minutes was delivered of full-term, living child, 7 lb. 15¼ oz., by low forceps. Central episiotomy. Third stage uneventful. Cervical inspection negative. Infant shows no anomalies. No cyanosis, convulsions, or snuffles. Moderate occipital caput. Measurements: length, 49 cm.; weight, 7 lb. 15¼ oz. Head: O.M., 13 in.; O.F., 11; S.O.B., 10; B.P., 9; B.T., 8. Treatment eyes, Credé; treatment cord, Credé."

The baby was breast fed with supplementary feedings. He nursed well and appeared and acted normally until the fourth day, at which time the head appeared slightly enlarged and the fontanelles full. During the next four days the head gradually increased in size, the fontanelles were bulging, and there was marked separation of all the cranial sutures. Small areas of ecchymosis appeared in the upper lids of each eye. There was a gradual loss of weight in spite of the fact that the baby retained all of his feedings. On Oct. 24, nine days after birth, the neurosurgical consultation revealed the following: temperature, 98° F.; pulse, 110; respiratory rate, 30. The baby was rather drowsy, but aroused easily and cried normally. The head was definitely enlarged, the greatest circumference being 14½ inches. The fontanelles were tense and bulging. All the cranial sutures were markedly separated. The frontal bosses were not prominent, and there was very little, if any, distention of the veins of the scalp. The upper lid of each eye showed ecchymotic areas at the inner and upper margins of the orbit. There was slight, but definite, cervical rigidity. The pupils were moderately dilated, equal, and reacted to light. The fundi were normal, the vessels full, and there was no choking. There was no facial weakness. The mucous membranes of the mouth

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TOMA IN INFANT 2 WEEKS OLD WITH
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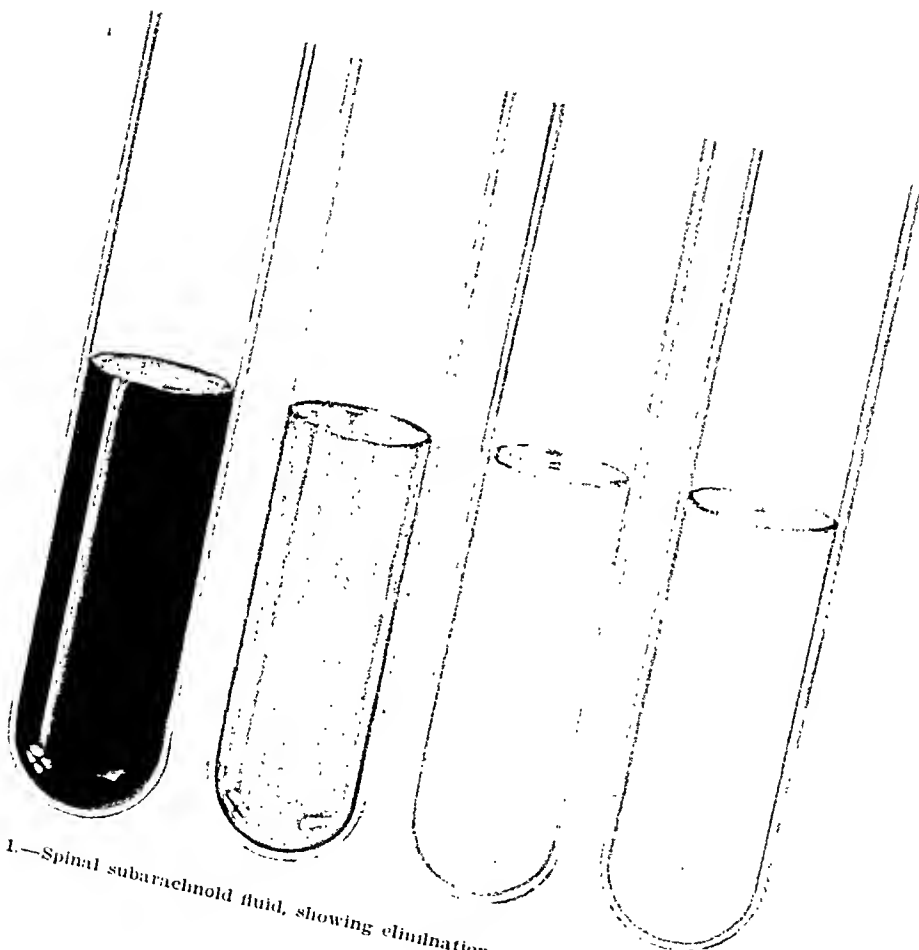


Fig. 1.—Spinal subarachnoid fluid, showing elimination of blood by spinal drainage.

out the course in the hospital. The fontanelles remained soft and the marked separation of the sutures gradually disappeared. X-ray examination of the skull at the time of discharge from the hospital showed the sutures to be normal (Fig. 3). The baby was discharged from the hospital on Nov. 29, 1939, twenty-eight days after operation, having made a complete recovery (Fig. 4).



Fig. 4.—Photograph of patient three months after operation.

COMMENT

Although there was no definite history of trauma in this case, the ecchymosis of the upper lids and the presence of a moderate occipital caput would lead one to suspect that slight trauma was the most likely etiologic factor. The prompt disappearance of blood in the lumbar subarachnoid fluid following daily lumbar punctures and the continued evidence of increased intracranial pressure indicated a coexisting lesion. Subdural hematoma was ruled out over the cerebral hemispheres by subdural taps through the coronal sutures. Ventriclelography definitely located the lesion in the posterior fossa. From this case, I am fully convinced that early investigation of the subdural space and ventriclelography are of prime importance in respect to diagnosis and localization. Delay may result in serious damage to the rapidly developing brain, especially when the clot is in the posterior fossa. Evacuation of the clot through a small trephine opening was selected (1) because of the

Operation (Nov. 1).—Ether anesthesia; cerebellar position. Through a small semielliptical incision over the occipital region, the occipital bone over the right cerebellar hemisphere was exposed in the usual manner. A small perforation was made in the bone and this opening enlarged to expose the underlying dura, which presented the typical bluish appearance of an underlying clot. The dura was then carefully incised, exposing the outer wall of the sac of a subdural clot. The cyst wall was well formed, the outer wall adherent to the under surface of the dura and grayish in color. When the sac was incised, 25 to 30 c.c. of dark, reddish brown, rusty-looking fluid escaped. No solid clots were seen. Following the evacuation of the clot, close to the midline the arachnoid, forming the posterior wall of the cisterna magna, could be seen bulging to the mesial side of the sac membranes. The bulging arachnoid was pricked with a needle, releasing clear, slightly xanthochromic fluid. The sac was irrigated with saline solution and the incision closed in layers in the usual manner, without drainage. The baby stood the operative procedure well, and immediately following the operation the fontanelles were sunken and there was a marked decrease in the separation of the sutures.

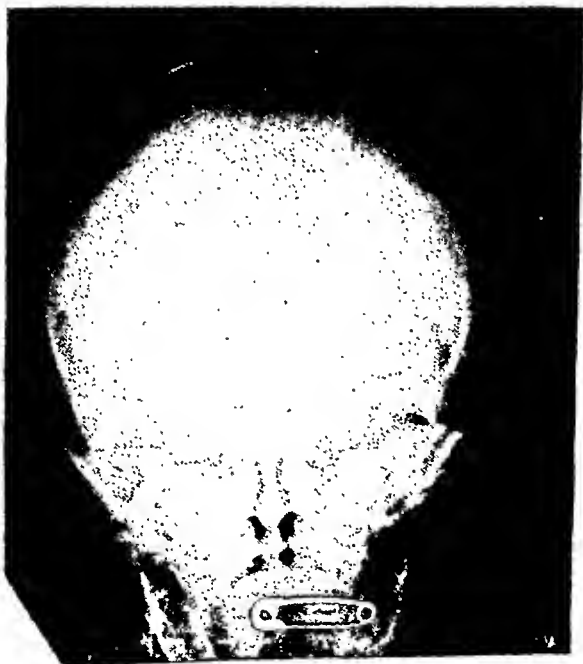


Fig. 3.—X-ray of skull on discharge from the hospital on Nov. 29, 1939, showing normal sutures.

Postoperative Course and Treatment.—The infant was given 50 c.c. each of citrated blood and 0.9 per cent sodium chloride solution immediately after the operation, and this was repeated five and one-half hours later. Ventricular and lumbar punctures were done twelve hours after the operation. Slightly xanthochromic fluid was obtained from both the ventricles and the lumbar subarachnoid space. Infusion of 0.5 ounce of salt solution and 15 c.c. of glucose was given every half-hour for twenty-six hours, beginning two hours after operation. The postoperative course was uneventful. The temperature twelve hours after operation rose to 102° F., but was normal twelve hours later and remained so through-

NOTE ON STRAIGHTENING THE HYPOSPADIAC PENIS

C. D. CREEVY, M.D., MINNEAPOLIS, MINN.

(From the Urological Division of the Department of Surgery at the Medical School of the University of Minnesota)

THIS brief paper has been prompted by recurring statements in the literature to the effect that Duplay's plastic operation, devised in 1874, is inadequate for correcting the ventral enrature of the penis associated with hypospadias; such a statement is usually accompanied by a description of a new method of dealing with the penile skin.

Correction of the deformity depends not upon what is done to the skin, but upon complete removal of the fibrous band beneath the corpora cavernosa. This band undoubtedly represents a rudimentary corpus spongiosum urethrae which, by its shortness and attachment to the intact urethra behind, to the corpora cavernosa above, and to the glans penis in front, serves as the bow string which produces the characteristic ventral curvature of the penis.

Duplay excised this fibrous band through a transverse incision between the external meatus and the glans, and closed Buck's fascia and skin longitudinally. Dissatisfaction with the results of this method led Hagner to correct the curvature by implantation of tubular Thiersch grafts transversely in the fibrous band between the corpora cavernosa and the ventral skin; these were later cut through to the ventral surface of the penis. Edmunds devised a two-stage operation in which a transverse buttonhole was made in the foreskin at the first session. Later the fibrous band was excised and the divided foreskin was utilized in a plastic closure. McIndoe has recently stated that this method is often required because of the inadequacy of Duplay's operation. Borchers has recently advocated slipping the penis under a double-ended pedicle graft of abdominal skin just above the symphysis. The ends of this flap are divided later. McKenna has excised the fibrous band and implanted a pedicle graft from the scrotum into the defect on the undersurface of the penis.

The methods of Hagner, Edmunds, and Borchers involve two operations; those of Borchers and McKenna leave hairy skin in the area from which the urethra must be constructed; Cabot has found that the hair may continue to grow and become encrusted with urinary salts. Duplay's method has neither of these disadvantages and, when properly done, achieves results as good as, or better than, any other procedure. There is always plenty of skin on the hypospadiac penis to permit complete straightening if the fibrous band is excised completely, so that the type of skin plastic is of very little moment.

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age of the infant and (2) because we know it is not necessary to remove the entire sac to effect a cure.

CONCLUSIONS

1. Subdural hematoma in the posterior fossa in infants is rare, but can and does occur and should be kept in mind as a possibility in all cases of hemorrhage in the newborn.

2. In infants early bilateral subdural taps through the coronal sutures are justified and indicated to rule out subdural bleeding, especially where there are signs of rapidly increasing intracranial pressure.

3. Ventriculography is a definite aid to localization, especially when the clot is in the posterior fossa.

4. A symmetrical dilatation of the ventricular system develops when the clot obstructs the flow of the cerebrospinal fluid from the ventricles.

5. Evacuation of the clot through a small trephine opening without drainage effected a cure in this case. It is a simple procedure which can be used to verify the diagnosis and to evacuate the clot at the same time.

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apparent in several of my own cases in which some curvature of the penis remained despite complete excision of the band, but disappeared after separation of the urethra from the corpora cavernosa.

Since Duplay's method of removing the remnant through a transverse incision between the meatus and the glans gives adequate exposure for carrying out this separation, and since longitudinal closure of this incision always leaves plenty of skin on the ventral surface of the penis, there is no need to employ the two-stage operations of Edmunds, Hagner, or Borchers, or the one-stage method of McKenna with its use of hairy skin.



Fig. 2.—A. L. before operation on Sept. 8, 1939.

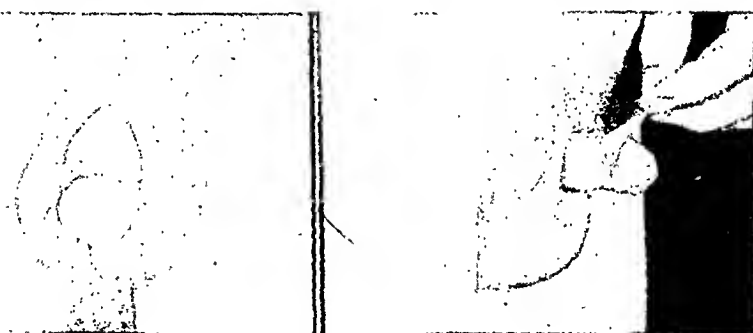


Fig. 3.—A. L. two weeks later.

The result obtained in the most recent of a series of twenty cases of hypospadias will serve to support this contention. The patient, A. L., University Hospital No. 669866, aged 15 years, had the most extreme form of curvature that occurs with hypospadias (Fig. 2). It was corrected by Duplay's method, modified only by extending the end of the transverse incision in the skin anterolaterally along the ridges which marked the transition between penile skin medially and scrotal skin laterally. Fig. 3 demonstrates that perfect straightening has been obtained in one stage despite the extreme deformity; the ventral surface of the penis is covered by hairless skin from which it is intended later to construct a new urethra by the method of Thiersch and Cecil.

An additional factor in production of the curvature is the fact (which is rarely mentioned in the literature) that the transition from normal urethra behind to fibrous rudiment in front is often gradual rather than abrupt. That is, in the majority of cases of hypospadias, the terminal portion of the intact urethra has a wall thinner and shorter than normal and so itself contributes to the ventral curvature of the penis.

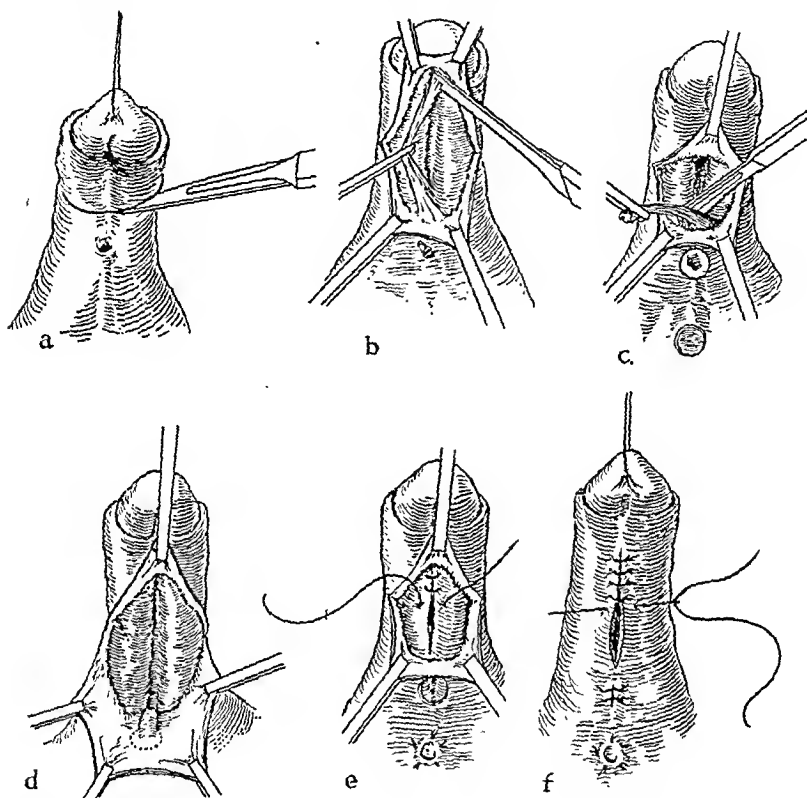


Fig. 1.—Duplay's plastic operation, with the addition of freeing and posterior displacement of the urethra.

- a, Incision;
- b, freeing of the fibrous band;
- c, removal of the band and preparation for posterior displacement of the external meatus;
- d, urethra for some distance behind the meatus has been freed from the corpora;
- e, posterior displacement of the meatus and closure of the fascia;
- f, closure of the skin.

In order to correct this curvature it is therefore essential not only to remove absolutely all of the band from the posterior edge of the glans penis to the external urinary meatus, leaving the tunica albuginea of the corpora cavernosa in this area completely bare, but also, as I have previously pointed out, to free the intact but deficient terminal portion of the urethra from the corpora until the penis can be straightened without traction (Fig. 1). In the more extreme types this may mean separating the urethra entirely from the penis. This has been perfectly

apparent in several of my own cases in which some curvature of the penis remained despite complete excision of the band, but disappeared after separation of the urethra from the corpora cavernosa.

Since Duplay's method of removing the remnant through a transverse incision between the meatus and the glans gives adequate exposure for carrying out this separation, and since longitudinal closure of this incision always leaves plenty of skin on the ventral surface of the penis, there is no need to employ the two-stage operations of Edmunds, Hagner, or Borchers, or the one-stage method of McKenna with its use of hairy skin.



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SUMMARY AND CONCLUSIONS

1. The single stage plastic operation of Duplay, devised in 1874, is, if properly performed, adequate for complete straightening of the most extreme degrees of ventral curvature occurring with hypospadias.

2. Success depends, not upon the type of incision and closure of the skin, but upon complete excision of the fibrous rudiment of the corpus spongiosum urethrae, supplemented, when necessary, by freeing and posterior displacement of the intact urethra.

3. An illustrative case (from a series of twenty) is reported.

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HYPOSPADIAS

HERBERT WILLY MEYER, M.D., NEW YORK, N. Y.

(From the Lenox Hill Hospital)

HERE are presented two cases of penoscrotal hypospadias in which the patients were operated upon nine and five years ago, respectively. The first patient was operated upon in 1930 shortly after McWhorter had published the method he employed successfully.¹ This method was based upon principles devised by Russell and published in 1900.² Thompson improved upon this method and in 1917 published his procedure.³

Operations for severe hypospadias are notorious for the difficulty in effecting a cure. Innumerable procedures have been devised and can be found in textbooks and in the literature. The late results were usually so uniformly poor that many surgeons abandoned operative therapy.

The first of our two patients was presented as a cured case before the New York Surgical Society in the fall of 1933, and the case was briefly described in the *Annals of Surgery* in 1934. In 1933 Lyle⁴ published a method which had been devised by the French surgeon Ombrédanne. This operation is called the Ombrédanne pouch operation. It is a splendid method and at the time of our first operation was not known in the United States. It gives such excellent results that I believe it has been generally accepted by surgeons. Having obtained a most satisfactory result, however, in our first case by McWhorter's method, we naturally handled a second similar case by the same method, eight months previous to the appearance of Lyle's paper. This second patient has also obtained a satisfactory result and therefore it seems permissible once more to draw attention to the procedure which was employed in these two cases.

The operation is somewhat more complicated than the Ombrédanne pouch operation. The latter does not require a preliminary suprapubic cystotomy during the plastic repair. The advantage is partly effaced in my opinion by the fact that the final cosmetic and esthetic results are superior in the McWhorter procedure as compared to the Ombrédanne pouch operation. Certainly in some patients this is a point well worth considering. McWhorter advises a perineal urethrotomy in place of a suprapubic cystotomy. From experiences obtained in our two cases, I prefer the suprapubic cystotomy.

TECHNIQUE OF OPERATION

The operation is divided into two stages. The first stage consists in the release of the bent and bound-down penis and division of the fibrous bands holding it down in nature's attempt to bring the abnormal urethral opening at the base of the scrotum to the tip of the penis

(Fig. 1). A transverse incision must be made just below the glans penis as shown in Fig. 2. The fibrous bands are completely divided so that the penis can be extended. This transverse incision is sutured longitudinally, bringing *A* to *B* at the center of the defect. This then forms a normal shaft of the penis. The result of this procedure in the second case is shown in Fig. 9. Upon the completion of this first operation, the urethral opening is approximately 2 to 2½ inches from the tip of the penis.



Fig. 1.—Penoscrotal hypospadias. Probe has been placed in urethral opening.

Following this procedure one must wait a long time until all post-operative induration has completely subsided and the thick skin of the penis is again soft, pliable, well-nourished with blood, and otherwise entirely normal. This takes many months, and the longer one waits, the better is the prospect of success in the second stage of the procedure.

The second stage constitutes the construction of a new urethra. At this time a suprapubic cystotomy is performed as a preliminary procedure. The new urethra is a tube lined with skin, fashioned from the shaft of the penis and prepuce, which will connect the cutaneous opening of the urethra with the tip of the glans where the urethral opening normally should be. Part of this newly formed tube is buried subcutaneously and the distal part is buried within the shaft of the penis to emerge normally at the tip of the glans.

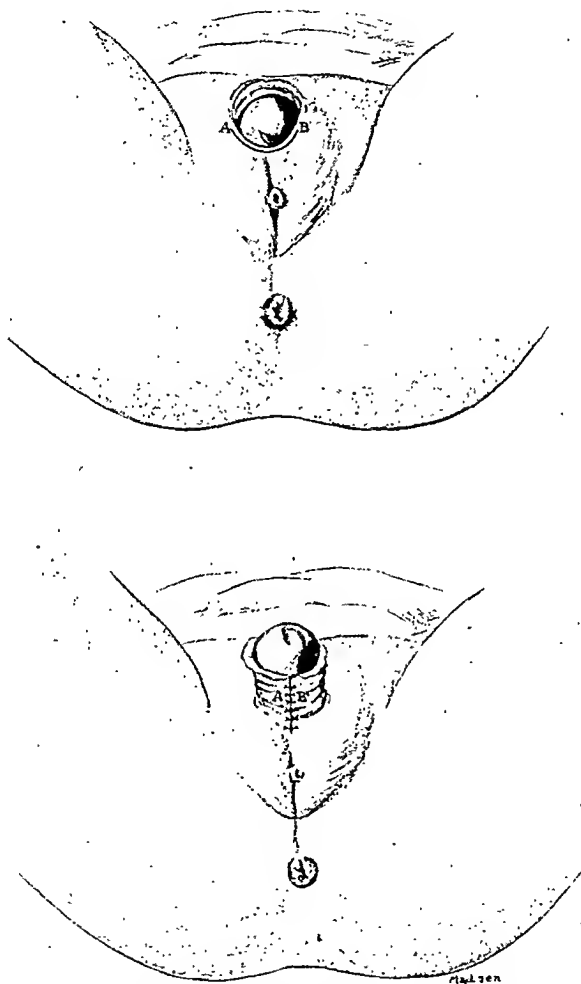


Fig. 2.—Diagrammatic drawing showing transverse incision made to free bound-down penis. A is brought to B in suturing the transverse incision vertically in order to form a shaft of the penis.

As shown in Fig. 4, a collar of skin is fashioned from the redundant prepuce, about 1 to 1.5 cm. wide, leaving it attached at the undersurface of the penis. This is lifted over the glans of the penis. The further lines of incision are parallel and run posteriorly to a point about

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In the first case we used fine needles and No. 000 catgut. No. 0000 catgut would have been better. From experience in this case and trouble encountered in the convalescence by the extrusion of some of the catgut knots, I advise the use of the finest needles and finest silk, such as are used in blood vessel surgery. This suture material comes

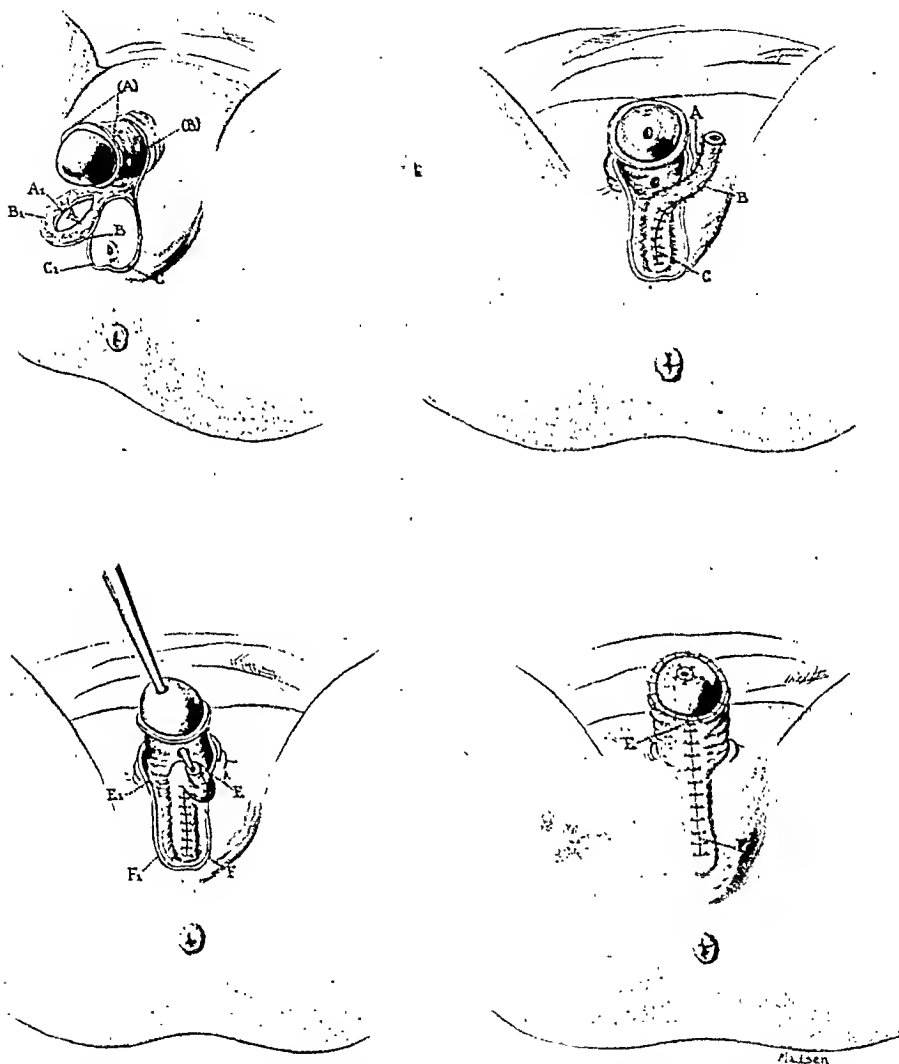


Fig. 4.—Showing the steps used to form the tubed urethral channel with skin on the inside. This tube as shown is drawn through the shaft of the penis and is then buried under the skin sutured over the tube.

all prepared and makes the smallest openings in the skin and allows better skin edge approximation.

The central opening in the collar of skin lifted off the prepuce is also sutured, thereby making an entirely closed canal and tube. At a

1 cm. behind the urethral opening. Here they are joined transversely. The incisions are deepened until they pass through the thin skin and are then dissected mesially along the shaft of the penis for a short distance only, leaving enough skin attached to the penis to furnish blood supply for the raised flaps. The remaining attached skin thereby forms the bed of the newly formed tube, while the raised portions form the lateral walls and roof of the urethra.

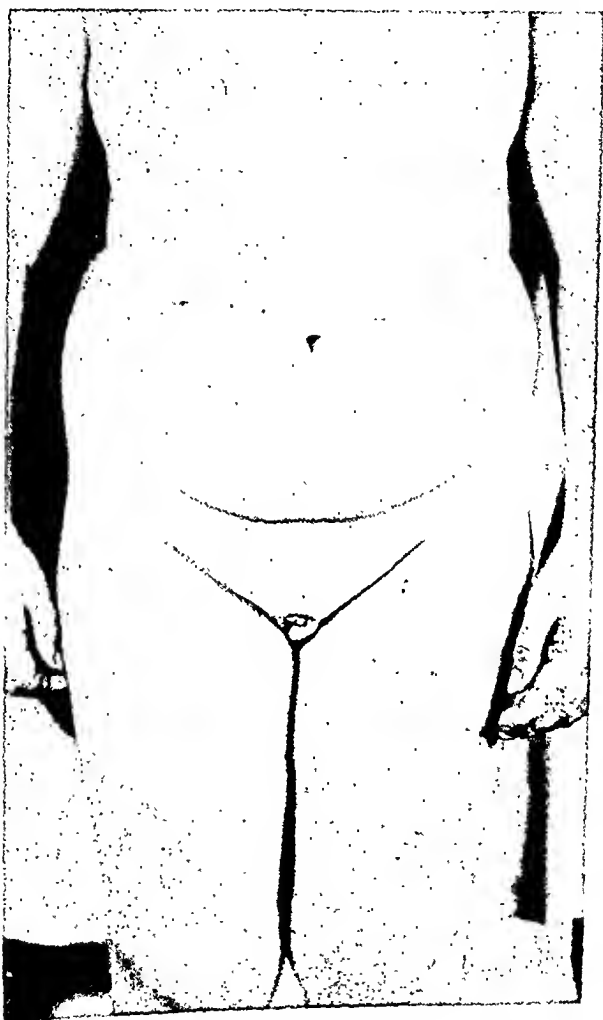


Fig. 3.—Case 1 before operation, showing undeveloped penis bound down. Note right undescended testicle.

By starting posteriorly and most meticulously suturing skin edge to skin edge with the knots inside, a tube is formed with skin on the inside and raw surface on the outside, slowly covering over and enclosing the urethral opening. The skin is, of course, very delicate (almost as thin as tissue paper) and is easily damaged and torn.

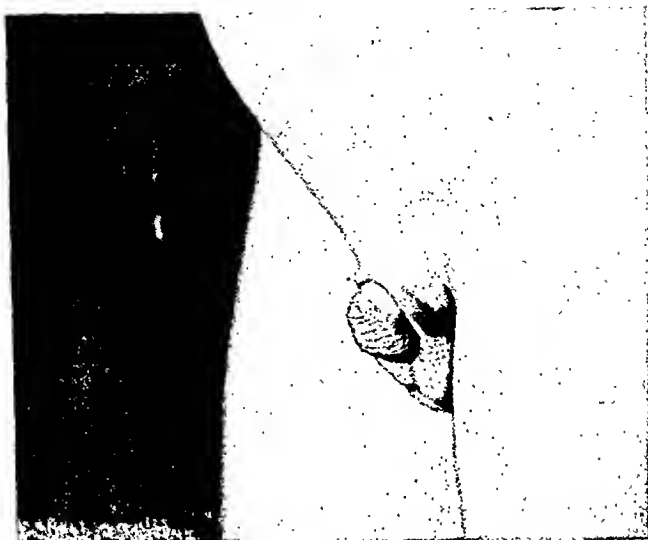


Fig. 7.—Case 2, showing the penis bent and bound down.

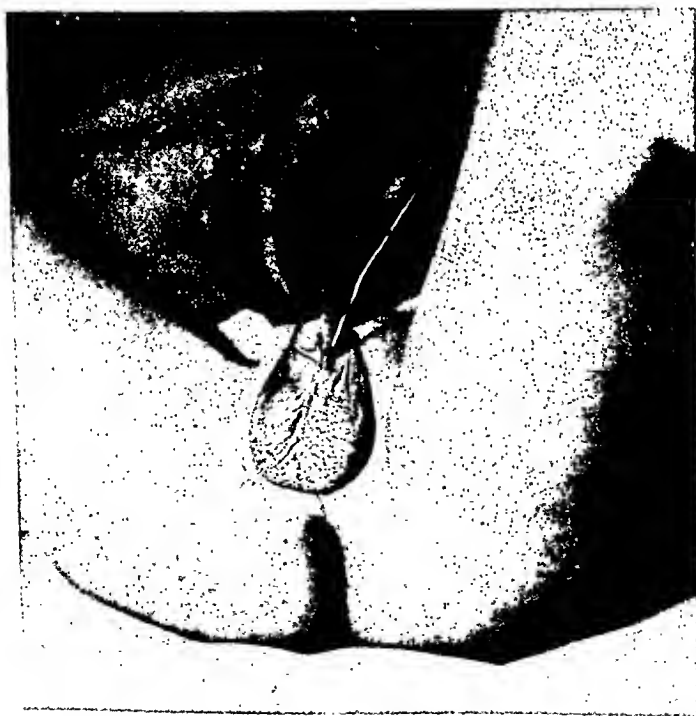


Fig. 8.—Case 2, showing probe placed in urethral opening. Note how nature tries to bring urethral opening to tip of penis.



Fig. 5.—Case 1 at end of operative repair. Shows excellent urethral stream emerging normally from tip of penis.



Fig. 6.—Same patient as shown in Fig. 5 nine years after operation at age of 18 years. Note that right testicle has descended. All functions perfectly normal.

point where this tube completely separates from the shaft of the penis, a canal is made through the shaft of the penis by plunging a narrow-bladed scalpel from the tip of the glans between the corpora cavernosa to the undersurface of the shaft of the penis, just in front of the attached portion of the newly formed tube. This canal is stretched with a small hemostat and the tube is pulled through this canal so that it emerges at the tip.

This urethral tube must now be buried and covered over with skin. This is done by undermining the lateral skin margins slightly and suturing these skin flaps across the tube with a most meticulous suture line in the center of the shaft of the penis. If there is any tension on the suture line, lateral or dorsolateral, relaxing incisions must be made through the skin of the shaft of the penis so that primary union of the



Fig. 11.—Case 2, showing excellent shaft of penis with stream of urine coming normally from tip of penis.

suture will ensue. These relaxing incisions will also help to avoid postoperative edema. The skin tube is allowed to emerge slightly beyond the surface of the glans and is cut obliquely to avoid circular stricture formation. A few sutures through the glans and tube edge will hold the tube in place and prevent it from drawing into the shaft of the penis.



Fig. 9.—Case 2, after first-stage operation. Shaft of penis has been formed, thereby bringing urethral opening formerly near tip of penis back at the bottom of shaft of penis at base of scrotum.



Fig. 10.—Case 2, at end of second-stage operation when urethral tube has been formed and buried under skin. Urethral sound has been passed into urethral tube all the way to the end, where urethra opens into newly formed tube.

AN IMPROVED APPARATUS FOR TIDAL DRAINAGE OF THE URINARY BLADDER AND EMPYEMA CAVITIES

CARROLL J. BELLIS, M.D., MINNEAPOLIS, MINN.

(From the Department of Surgery, University of Minnesota Medical School)

IRRIGATION OF THE URINARY BLADDER

NEUROGENIC Vesical Dysfunction.—Urinary sepsis, originating in the bladder and urethra and extending into the upper reaches of the urinary tract and gradually destroying the kidneys, is the most common and fatal sequel to spinal cord injury. The extending infection is directly attributable to either (a) repeated instrumentation of the urethra coincident with repeated catheterization or (b) interruption of the neurophysiologic cycle of intravesical pressure and urinary expulsion.

The accepted teachings of Sherrington¹ assign a postural tone to the normal detrusor muscle, permitting an isotonic filling of the bladder to a pressure of from 6 to 10 cm. water. When the intravesical tension is from 10 to 14 cm. water, desire to void is felt. The tension has been shown cystometrically to rise rapidly from that point so that, when the bladder contains from 200 to 400 c.c., a pressure of from 20 to 30 cm. water exists.

Neurogenic vesical dysfunction results from lesions of the brain, peripheral nerves, spinal cord, or of the intramural ganglia through injury or destruction of the centers for bladder function or of their afferent or efferent pathways. This occurs in central nervous system lesions such as tabes dorsalis, cord tumors, cord trauma, multiple sclerosis, subacute combined degeneration, syringomyelia, spina bifida, and infectious and traumatic myelitis. It is also seen in bilateral frontal lobe and caudate nucleus lesions. In neurogenic vesical dysfunction, desire to void is not felt until the intravesical pressure is higher than that normally adequate (Creevy^{2,3}). The resulting constant elevated pressure leads to capillary stasis in the bladder wall and atrophy of the detrusor muscle with retention through lack of expulsive force. At abnormally high intravesical pressures, bladder contractions expel urine without the attending desire to void, this state being known as paradoxical or overflow incontinence. The retained urine causes an additional pressure anesthesia of the bladder wall augmenting the degree of retention.

Creevy has recommended the use of conservative measures for the treatment of neurogenic vesical dysfunction. These are (a) voiding "by

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The circular denuded collar of the prepuce is now sutured just the same as one does in an ordinary circumcision. Detail and exactness in suture and gentleness in handling the tissues with the finest of instruments are vital for success in healing.

The suprapubic fistula should be used for fully twelve to fourteen days before any attempt is made to allow the patient to void or until any disturbance in wound healing has been completely overcome. If there should be any leak due to improper healing, a revision is required at the site of the leak. It is important, therefore, that the suprapubic fistula be maintained until one is sure of a successful outcome. In the aftercare it is wise to pass sounds through the skin tube for the first year or so at biweekly intervals in order to make sure that no stricture develops in the urethral tube (Fig. 10).

In the first case it is now nine years since operation. The young man has grown to manhood and every accompanying function has developed normally. The right undescended testicle (Fig. 3) suddenly descended into the scrotum during an attack of severe pain following some injections of antuitrin S. The urinary stream is perfectly normal (Fig. 5). Fig. 6 shows the present absolutely normal appearance of the external genitals.

In the second case it is five years since operation and this boy also is normal in appearance and function, but he is still in the adolescent period (Figs. 7-11).

Granting that the Ombrédanne pouch operation is possibly the simpler procedure with a greater probability of early success and shorter convalescence than the McWhorter type of operation, I still feel that the successful outcome of the cases described here warrants the addition of this procedure to the surgical armamentarium. Failure to cure a patient with marked hypospadias will only lead to unhappiness and inferiority complexes for the unfortunate individual.

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bladder. Recently, Myers¹² has described an automatic bladder irrigator which delivers a definite quantity of irrigant to the bladder, regardless of the intravesical pressure. Vary¹³ has described a somewhat complicated tidal irrigator which has many functional advantages. Munro and Hahn,^{14, 15} however, designed an excellent bladder tidal irrigator

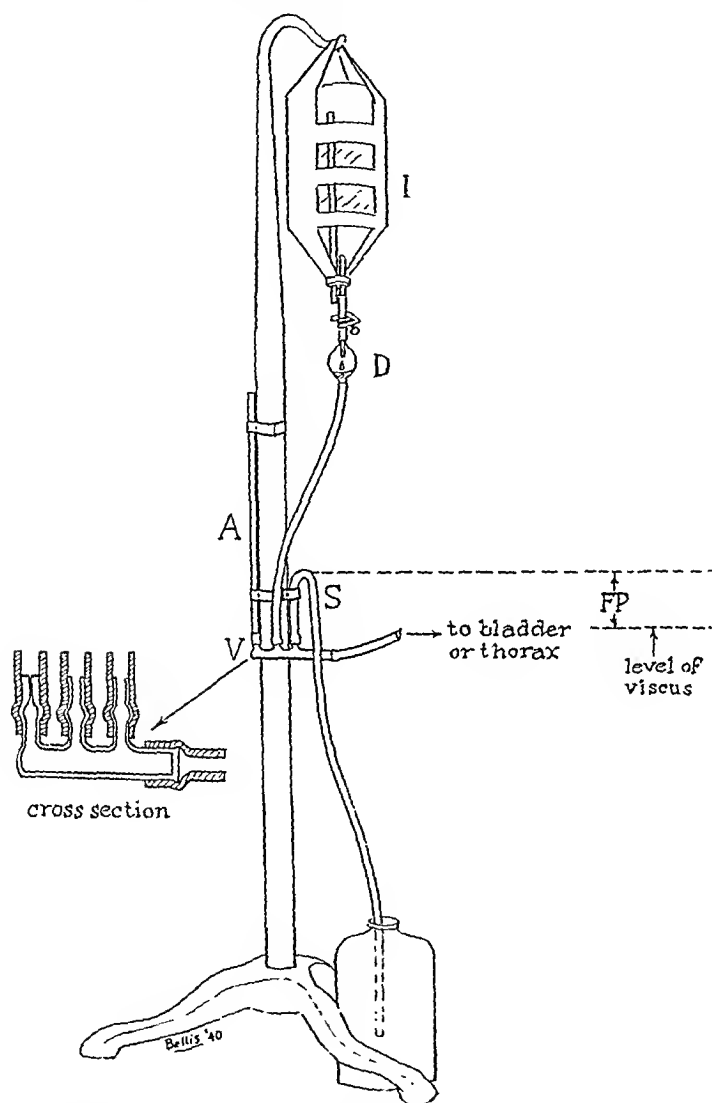


Fig. 1.—Tidal drainage apparatus. *I*, irrigant; *D*, drip regulated by screw clamp; *FP*, filling pressure at which siphon, *S*, will trip; *A*, air vent and manometer; *V*, valve made of fused outlet of glass Dakin's tube.

pre-eminently for use in spinal cord injuries. Through prompt use of this apparatus, they were able to reduce urinary sepsis in cord injuries from 73 to 15 per cent. The accurate adjustment of the component parts of their apparatus, however, and the difficulties often accompanying its proper function have often been troublesome.

the clock'' at regular and frequent intervals, (b) cholinergic drugs (eserine, pilocarpine, and acetylbetamethylcholine chloride), and (c) a combination of (a) and (b) with intermittent catheterization. Where complete bladder rest is desired, it is accomplished by cystostomy. In addition, he⁴ has pointed out that mechanical obstruction to urination so slight as to cause no symptoms in the normal bladder may lead to retention or overflow if only mild neurogenic dysfunction exists.

Cystitis.—Where the bladder has become secondarily infected due to an indwelling catheter or as a sequel to radium therapy for carcinoma of the cervix with a succeeding Wertheim operation, frequent irrigation of the bladder at low pressures is imperative. Often, however, cystitis is present in association with carcinoma of the cervix prior to therapy. Bladder infections produced through these or hematogenous agencies may be effectively treated by specific peroral chemotherapy where the etiological bacteria are identified. In addition, the local application of these antiseptics is beneficial when they are applied as irrigants. Regular frequent irrigations assist in removal of secretions and reapplication of fresh antiseptic solution.

THORACIC EMPYEMA

Carlson⁵ and Carlson and Bowers⁶ have emphasized that five principles govern the treatment of thoracic empyema:

1. Adequate drainage.
2. Avoidance of early open pneumothorax.
3. Rapid sterilization of the diseased area.
4. Early obliteration of the cavity by expansion of the lung.
5. Good medical care and nutrition of the patient.

In the meta- or postpneumonic types of thoracic empyema, aspiration is continued until the pus is too thick. Then dependent drainage is established through an intercostal catheter. Frequent irrigation of the empyema cavity facilitates the free drainage of pus, washes and sterilizes the cavity walls, and digests the exudate on the visceral pleura which restrains the lung in its natural tendency to re-expansion (Wangensteen⁷).

The use of a water-sealed snetion at a negative pressure of from 10 to 30 cm. water to re-expand the lung has been stressed by Wangensteen. Where the pleura is thick, adequate drainage by snetion alone cannot be obtained. Dilution of the exudate by an irrigating fluid renders the negative pressure more effective. Plugging of the intercostal catheter requires washing out of the catheter in situ or replacement. Heretofore, it has been the practice to manually irrigate and aspirate the intercostal catheter at frequent intervals.

APPARATUS

Hart^{8, 9, 10} and Davis¹¹ were among the first to suggest useful decompression and irrigating devices for thoracic empyema and the urinary

bladder. Recently, Myers¹² has described an automatic bladder irrigator which delivers a definite quantity of irrigant to the bladder, regardless of the intravesical pressure. Vary¹³ has described a somewhat complicated tidal irrigator which has many functional advantages. Munro and Hahn,^{14, 15} however, designed an excellent bladder tidal irrigator

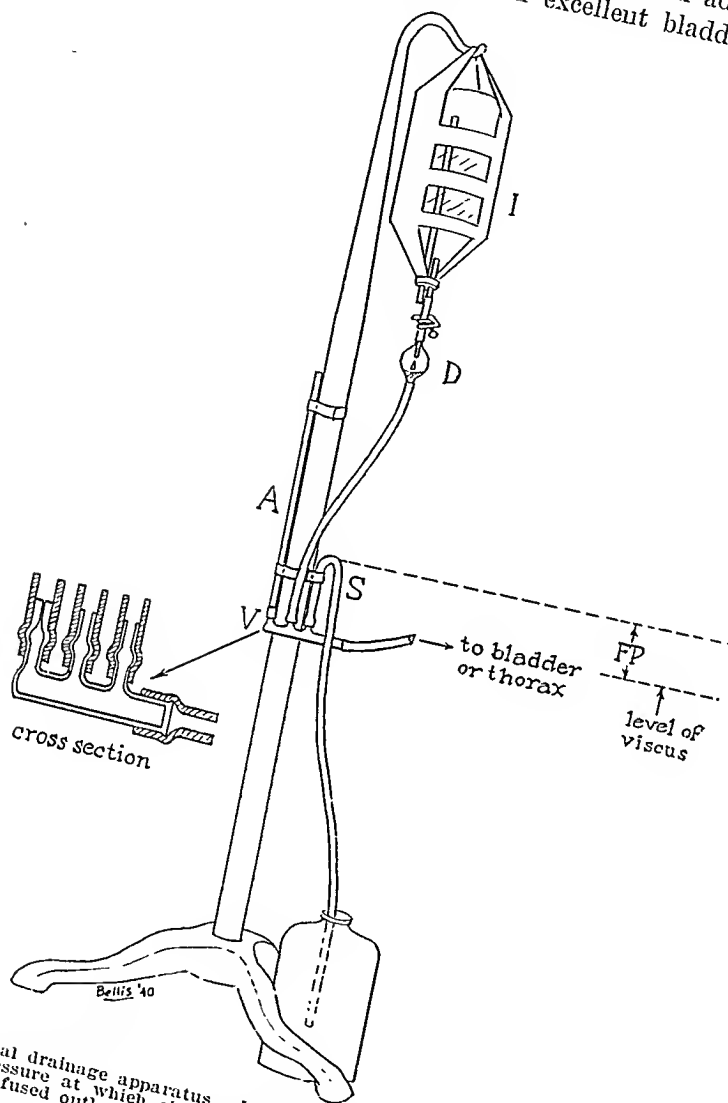


Fig. 1.—Tidal drainage apparatus. *I*, irrigant; *D*, drip regulated by screw clamp; *FP*, filling pressure at which siphon, *S*, will trip; *A*, air vent and manometer; *V*, valve made of fused outlet of glass Dakin's tube.

pre-eminently for use in spinal cord injuries. Through prompt use of this apparatus, they were able to reduce urinary sepsis in cord injuries from 73 to 15 per cent. The accurate adjustment of the component parts of their apparatus, however, and the difficulties often accompanying its proper function have often been troublesome.

In its place, the apparatus shown in Fig. 1, in use in the University of Minnesota Hospitals, is suggested for tidal irrigation of the bladder or empyema cavities. The irrigant (*I*) is placed in a suitable reservoir at least 75 cm. above the level of the cavity to be irrigated. It is delivered at the rate, usually, of from 40 to 60 drops per minute, the delivery being increased or decreased according to the frequency of desired drainage periods. The flow is regulated through the drip (*D*) by a screw clamp; the drip must not contain an air vent. Entering one vertical arm of a three-outlet glass Dakin's tube, the solution passes through the horizontal arm to the indwelling catheter. Through the other vertical arms, the irrigant is diverted, respectively, through a siphon (*S*) of flexible rubber intravenous tubing and a vertical glass tube (*A*) about 0.6 or 0.7 mm. in diameter which serves as an air vent and manometer. At the bottom of the air vent, a valve (*V*) is interposed. This consists simply of one of the glass Dakin's tube outlet tips which has been fused to a capillary of a diameter just sufficient to admit the point of a common pin. The height of the siphon is adjusted to the desired pressure (*FP*) at which the bladder or empyema cavity is to be filled to initiate siphonage by fastening its upper curve at the desired height above the bladder or intercostal catheter. The level of the pubis and the point of entrance of the intercostal catheter into the chest are respective convenient landmarks for zero points. The distal portion of the siphon empties into an open drain bottle.

The process in the ordinary course of events consists in a simultaneous flow of irrigant into the bladder or chest and up the proximal arm of the siphon to the level of the filling pressure at which the arch is set, and through the valve into the vertical air vent. When fluid overflows the arch, siphonage is instituted, rapidly draining the bladder or pleural cavity. However, fluid is siphoned from the air vent very slowly, due to the interposed valve. The viscus is thus emptied before the siphon is broken by air coming through the vent. By adjusting the rapidity of flow through the drip or the filling pressure, each cycle may be made to vary from a few minutes to one or two hours. The apparatus is functioning properly when respiratory excursions are visible in the air vent or in the proximal arm of the siphon. Where suction is to be instituted in thoracic empyema, the irrigator is discontinued, and the suction outlet is connected to the intercostal catheter.

A "reservoir," wasting its volume of irrigant at every cycle, is thus eliminated. In addition to the few connections, it is not necessary to give extraordinary attention to the size of the tubing. The opening in the valve must be so small that the viscus will empty before the vertical glass air vent is cleared during siphonage. The rubber connections are of ordinary intravenous tubing. If no glass Dakin's tubes are available, T-tubes of usual hospital or laboratory sizes may be used, and the glass portion of an eye dropper may be fused as a valve.

For the bladder the irrigant is ordinarily saturated boric acid solution, but may be replaced by silver nitrate, potassium permanganate, or other antiseptics for tidal irrigation of the infected bladder. In the latter case, only low intravesical pressures should be used, the siphon arch being elevated to not more than from 4 to 5 cm. above the pubis. For pleural irrigations, physiologic saline solution or Dakin's solution is commonly used at a filling pressure of less than 10 cm. water.

DISCUSSION

The common term "cord bladder" refers to a bladder which functions abnormally due to disease or injury of the spinal cord. This state is properly called neurogenic vesical dysfunction, and, in its management, tidal drainage diminishes the urinary sepsis attending the use of the indwelling catheter. According to Munro, these bladders pass through three definite stages if the lesion is above the sacral segments. Hematomyelia or edema at any level or incomplete cauda equina lesions introduce a fourth stage.

1. The *atonic* bladder is due to an areflexia occurring immediately after injury to the cord during the period of spinal shock. The capacity of the bladder allows extreme distention, the external sphincter being under neither voluntary nor reflex control. Tidal irrigation at an intravesical pressure of from 2 to 5 cm. water is recommended here.

2. The *autonomous* bladder invariably follows the first stage, and, in addition, is the end stage in complete destruction of the sacral cord or cauda. Despite the persisting external areflexia, the intramural reflex control of the detrusor muscle and internal sphincter allows intermittent emptying with a storage capacity less than that of the atonic bladder. Central inhibition is, of course, absent here, and tidal irrigation at an intravesical pressure of from 10 to 15 cm. water is recommended.

3. The *hypertonic* bladder is manifest in all cord injuries except those of the sacral segments and cauda. The segmental spinal reflex activity has been re-established in an uncontrolled manner, the bladder emptying at irregular intervals. The storage capacity is less than that of the autonomous bladder.

4. The *uninhibited reflex* bladder operates independent of central inhibition of which it has been deprived. It empties incompletely through a local stretch reflex, the retention favoring a tendency toward total reversion to the *atonic* bladder.

The differential diagnosis of these types is made by cystometry, the cystometrograms being easily made with the apparatus described herewith and compared with the normal curve. By varying the intravesical pressure of the tidal irrigator as the bladder passes through the stages outlined, urinary stasis is obviated and the infection consequent to the indwelling catheter circumvented.

In thoracic empyema, adhesions forming between the visceral and parietal pleura contribute resistance against collapse and mediastinal shift produced by the positive pressure of the atmosphere. When this stage has been reached, signaled by the changing of thin pus to highly viscid exudate, intercostal catheterization or open drainage may be safely instituted. We have found such pus to contain from 50 to 80 per cent protein.

Tidal irrigation assists in diluting the thick pus and in its removal. It contributes to sterilization of the cavity by frequently washing away secretion and introducing antiseptics. Only in this manner must it be considered as aiding in re-expansion of the lung. In a somewhat similar manner, blowing exercises aid in re-expansion of the lung. The increased intrapulmonic pressure attending blowing against resistance has no effect whatever upon the intrapleural pressure of the thoracotomized side. Its only asset lies in the fact that during the act it maintains the lung distended while the contraction of the thoracic expiratory muscles decreases the volume of the pleural space and forces pus through the thoracotomy. Thus, blowing exercises have their only virtue in very slightly stretching adhesions during the preliminary deep inspirations, facilitating mobilization of the lung. Drainage, irrigation, or blowing exercises are virtually ineffective in re-expanding the lung, a task effectively discharged by continual suction applied to the indwelling thoracic catheter.

SUMMARY

The effects of neurogenic vesical dysfunction upon the emptying mechanism of the bladder are described insofar as the physiology of micturition is known. The neurophysiologic alterations of the detrusor muscle and sphincter control attending spinal cord injuries are briefly reviewed. The effects of irrigating thoracic empyema cavities are enumerated, and the advantages are discussed. A simplified apparatus for tidal irrigation in neurogenic vesical dysfunction, for irrigation of the infected viscous with undisturbed central control, or of thoracic empyema cavities is described.

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PERINEAL PROSTATECTOMY

A MODIFICATION OF CLOSURE

SAMUEL A. VEST, M.D.,* UNIVERSITY, VA.

(From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital, Baltimore, Md.)

IN A recent publication¹ I have reported a series of 365 consecutive prostatic operations with a mortality of 1.6 per cent. It was felt that this mortality was particularly significant because the patients were on a public ward and a good percentage were unusually poor candidates for any type of operative procedure. The average age was well over 60 years. It was further significant that the operations were performed entirely by the resident house staff, who were receiving their first operative training and experience. It was pointed out that perineal prostatectomy, suprapubic prostatectomy, and transurethral removal of the obstructing prostate each has its place and that, if the indicated operation in each individual case is carried out instead of a stereotyped procedure, the maximum satisfactory results would be obtained. In general, the size of the obstructing prostate was the determining factor in the selection of either open operation, perineal or suprapubic, or transurethral, using the original Young punch or Thompson's modification, or the McCarthy resectoscope. In the treatment of patients presenting the average size or above prostatic hypertrophy, prostatectomy was carried out in 233 of the 365 cases and in practically all instances this was perineal prostatectomy.

The advantages of removing medium- and large-sized adenomas by the perineal route, such as visualization of the operative field with satisfactory control of hemorrhage, dependent drainage, putting the bladder at rest to minimize upper tract infection, etc., have often been stressed by Young² and others. The results published by us recently from the ward service have again served to emphasize the advantage of the perineal removal of enlarged prostates according to the technique of Young as an extremely valuable procedure in a large percentage of cases.

It is the purpose of this publication to present a modification of closure in perineal prostatectomy which I found advantageous in certain instances during my tenure as resident in the Brady Urological Institute.

One of the most formidable complications of surgical removal of the prostate, to be avoided whenever possible, is postoperative hemorrhage. Postoperative hemorrhage following perineal prostatectomy for obvious reasons is the least likely complication as compared with either supra-

*Lalor Fellow in Urology, Johns Hopkins University.
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pubic or transurethral procedures. Continued hemorrhage following transurethral resection with blockage of the catheter by clots results in distention of the bladder, and technical procedures to aspirate and free the bladder of blood may result in infection, pyelonephritis, and other serious complications. Continued hemorrhage following either perineal or suprapubic prostatectomy may also sometimes necessitate aspiration and irrigation and even reopening the incision and insertion of packs into the vesical orifice. Such a complication may be followed by shock, or local infection of the wound or bladder with delayed healing and actually acute or subacute pyelonephritis and septicemia. It is possible that marked hypertension with rigidity of the walls of the arteries supplying the prostate might tend to prolong bleeding following removal of the adenomatous prostate. There seems indeed to be considerable variation in the vascular supply of individual prostates. In some cases complete removal of a large adenoma by the perineal route is practically bloodless, while an identical case will show a tendency to considerable vascular oozing, necessitating suturing the vesical neck, packing of the wound, or insertion of various types of traction bags. The majority of the bleeding following perineal prostatectomy seems to come from the margin of the vesical orifice which is well illustrated in Fig. 1. Bleeding from the prostatic capsule or from the prostatic tissues is usually slight and of no consequence.

One of the main advantages of perineal prostatectomy is that the operation is carried out under vision and it is not difficult to determine the source of hemorrhage. I have yet to encounter any hemorrhage which has not been readily controlled at operation except that from the margins of the retracted vesical orifice. By use of proper methods, one of which is described here, hemorrhage following perineal prostatectomy can be kept to a minimum or entirely controlled. In the recent report referred to above, transfusion because of postoperative hemorrhage was necessary in only 4.7 per cent of the cases following prostatectomy.

The prevalent method of controlling hemorrhage following prostatectomy on the ward service six years ago was either by packing the vesical orifice with gauze or by means of a Davis traction bag. These methods have gradually been abandoned in favor of simple sutures into the vesical orifice so as to approximate the vesical orifice to the prostatic capsule. Statistics on the ward service in about 500 cases have shown that in the hands of the residents there have been distinctly better results with less complications and shorter healing time of the perineal wound if the vesical orifice was sutured. With this apparent distinct advantage following the use of sutures, the only complication I have been able to discern has been occasional postoperative hemorrhage which has sometimes necessitated packing or insertion of a rubber bag into the wound. This hemorrhage apparently occurs from the margin of the vesical orifice and is due to failure of the type of sutures used. The

sutures for the most part have been simple sutures approximating the various quadrants of the vesical orifice to the prostatic capsule in such a way as to pull the vesical orifice against the capsule, thus simulating normal relationships. The failure of the sutures in rare instances has

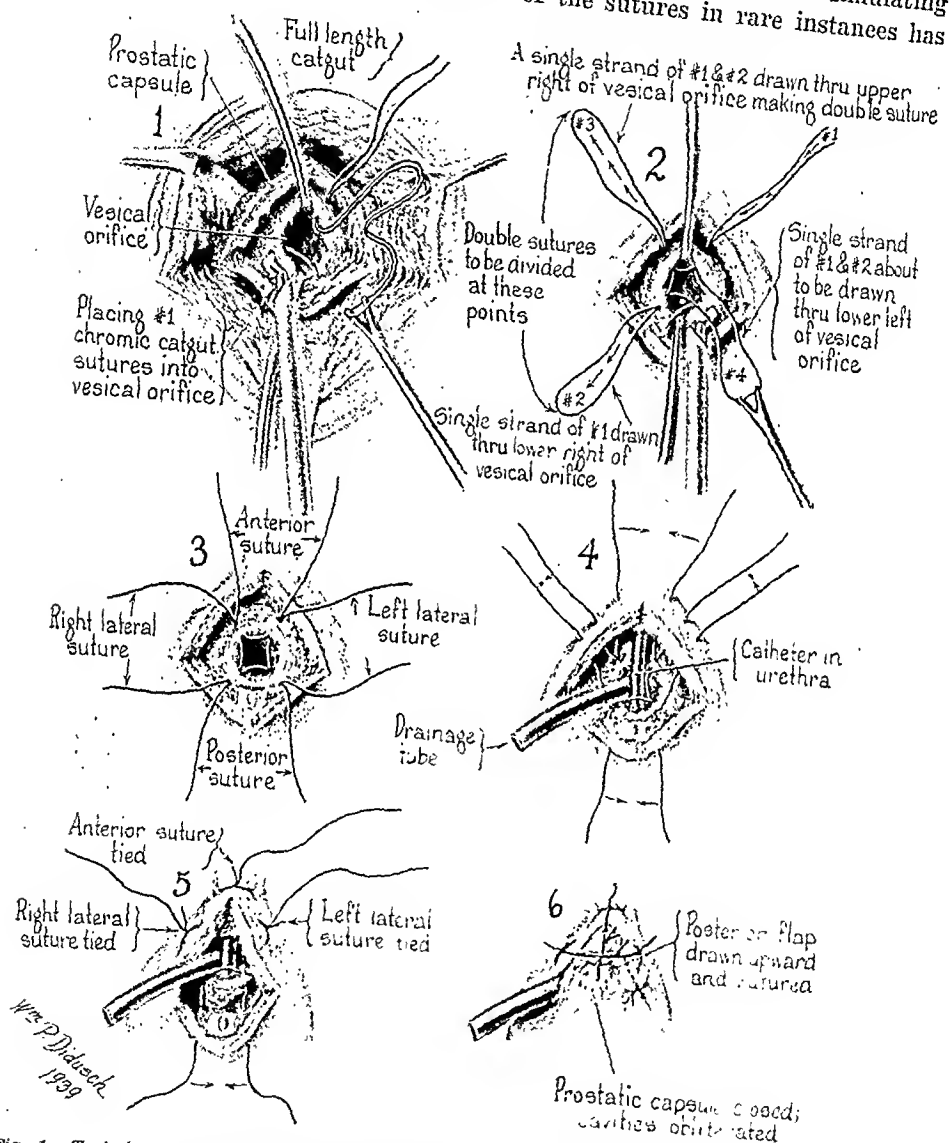


Fig. 1.—Technique of reconstructing the vesical orifice to eliminate hemorrhage following removal of benign prostatic hypertrophy.

been due to the fact that they did not circumscribe the vesical orifice in its entire 360 degrees so that, when hemorrhage occurred, it was probably due to a small spurting vessel between two sutures. With this in mind, I have modified the closure so that the full 360 degrees of vesical

orifice is included by the sutures. At the same time these modified sutures have reconstructed the vesical orifice in a manner similar to that present in the normal. A description of the technique is as follows:

Routine perineal prostatectomy, according to the technique described by Young, has been carried out in the clinic and needs no reiteration here. It should be emphasized, however, that, in order to facilitate the proper use of the sutures, the surface of the prostatic capsule should have adequate exposure and the inverted V-incision should be slightly wider and larger than usual. This makes the placing of the sutures, to be described, less difficult. Fig. 1 shows the various steps I have found advisable in cases in which there seems to be an unusual amount of vascularity at the vesical orifice in order that postoperative hemorrhage may be kept to a minimum or entirely controlled. In Fig. 1, 1 shows the prostatic cavity immediately following thorough removal of a large adenoma. The vesical orifice is pulled well into view by two long tenaculums which have grasped it anteriorly and posteriorly. The adenoma has been cleanly cut from the vesical orifice and posterior urethra by means of scissors.

By means of a boomerang needle, the long double suture of No. 1 plain catgut has been pulled through the vesical orifice in the region of 2:00 o'clock. This suture is shown with Young's boomerang needle just before grasping it and pulling the same suture through the vesical orifice in the region of 8:00 o'clock. These sutures are taken rather deeply into the vesical orifice so that they will include any retracted open vessels that might be on the bladder side. The placing of this suture may be sometimes awkward because a complete length of catgut, even though doubled, is not quite long enough. This can be remedied by tying two lengths together before beginning the procedure. In Fig. 1 (2) the double suture has now been pulled through the vesical orifice both in the region of 10:00 and of 8:00 o'clock, following which a single strand of the double suture which transverses the vesical orifice has been grasped and pulled through the vesical margin in the region of 10:00 o'clock and the boomerang needle is shown in the act of pulling the remaining strand across the vesical orifice through the margin in the region of 4:00 o'clock, following which the sutures are divided at the points labelled 2, 3, and 4. The situation after these sutures have been cut is shown in Fig. 1 (3). There are shown four individual sutures at the vesical orifice which are indicated as anterior, posterior, right and left lateral. As will be seen in 3, each strand of the left lateral suture, for example, goes through the same needle hole in the vesical orifice as the adjacent anterior and posterior suture, so that no vesical orifice margin is left between in which there might exist a spurting artery. The four sutures, therefore, include the entire 360 degrees of vesical orifice. In Fig. 1 4 these four sutures have been pulled through the corresponding areas in the prostatic capsule, following which a

urethral catheter and a small perineal drainage tube are shown in place. It will be noted that the anterior suture has been placed far anteriorly in the prostatic capsule so that when it is tied the anterior lip of the vesical orifice is pulled down on the anterior surface of the catheter and the anterior margin of the vesical orifice will then very closely approximate that of the divided urethra. The portion of the prostatic cavity where the anterior prostatic commissure and urethra once existed is thus obliterated. The lateral sutures are next tied as shown in Fig. 1 (5). The last procedure is to tie the posterior suture which ligates the ejaculatory ducts. After tying the sutures, a single strand of each is divided as shown in Fig. 1 (5). In 6 it can be seen that the single strand of posterior suture has been tied to the anterior and the two laterals have been tied across the midline. The tying of the posterior to the anterior has carried forward the tip of the inverted flap and reapproximated it into its original position with the tube coming out one of the limbs. Sometimes a small single suture is placed on the opposite side of the V as shown in Fig. 1 (6) to close completely the prostatic capsule except at the point where the tube emerges. With this type of closure the vesical orifice is thoroughly circumscribed in its 360 degrees and is pulled down into the cavity of the prostatic capsule, very near to the stump of the membranous urethra. This tends to produce early obliteration of the prostatic capsule and leaves only a very short bridge for the regenerating mucosa of the vesical orifice to transverse before it meets the mucosa of the membranous urethra. The perineal tube is withdrawn at the end of twenty-four or forty-eight hours according to whether or not perineal drainage is necessary because of infection, etc. The remainder of the perineal wound is closed according to the usual technique, which consists of pulling the levator ani muscles together with plain catgut and suturing the perineal skin with interrupted waxed silk or catgut sutures.

Numerous methods for handling the vesical orifice, prostatic capsule, and perineal wound by means of sutures, all of which have undoubtedly given good results, have been reported by Young, Wildbolz, Hinman, and others. In my hands the present technique has been very satisfactory and it is believed to eliminate greatly the possibility of hemorrhage and at the same time to effect a normal anatomical reconstruction of the prostatovesical relationships. I have had no difficulty in inserting sutures according to the method described and the entire operation, in most cases, has been carried out in about thirty minutes. There has been no postoperative hemorrhage in any instances and this type of suture has in no way interfered with proper and rapid healing of the perineal wound. The first thirteen cases in which I used this method were included in the recent report on prostatic mortality. The average healing time for the perineal fistulas was 13.5 days, following which each patient voided freely with complete control. In one case I cysto-

scoped a patient on the eighteenth day with both the Young and McCarthy cystoscopes and found the mucosa and vesical orifice to be normal in every way except for some hyperemia. There were no denuded areas between the membranous urethra and the bladder and entire healing of the mucosa of the prostatic urethra had taken place by the eighteenth day. The procedure has been carried out a number of times in private cases with entirely satisfactory results and it is advocated as a valuable method following perineal removal of the benign prostate in cases where there seems to be an unusual amount of vascularity and tendency to hemorrhage.

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THE PRINCIPLES AND THE PRACTICE OF THE RADICAL OPERATIONS FOR HERNIA

PROF. DR. EUGENE PÓLYA, BUDAPEST, HUNGARY

I. GENERAL PRINCIPLES

THE main purpose of every radical operation for hernia is to restore the integrity of the abdominal wall and its resistance in places where it is likely to yield to intra-abdominal pressure. There are generally defects of the musculature or the aponeurotic structures, or both, where the resistance of the abdominal wall to intra-abdominal pressure is impaired. Indirect inguinal hernias not infrequently deviate from this rule. The muscles are well developed and the aponeurosis faultless so that even large hernias of this kind can be cured by high ligation and removal of the sac alone (Kocher's method). Frequently, however, one finds weak muscles and an unsatisfactory aponeurosis even in congenital hernias, and then cure by simple ligation of the sac is impossible. In these cases of indirect inguinal hernia the reconstruction and strengthening of the abdominal wall is as necessary as it always is in direct inguinal and in all other forms of hernias.

The closure of the defect of the abdominal wall is undoubtedly the most important part in the radical cure of the hernia, but the extirpation of the hernial sac and its high ligation must generally precede it. However, the latter procedure may be unnecessary in cases in which there is only a diffuse protrusion of the peritoneum. In such cases even the opening of the peritoneum can be avoided, but the protruding peritoneum must be carefully freed of all its adhesions, and the margins of the hernial defect of the abdominal wall clearly exposed before its closure is begun.

The closure of the abdominal defect ensures radical cure only when it is complete and when the permanency of the broad contact of the structures united by the sutures is assured.

In order to do this, the following rules must be constantly regarded:

1. Avoid all tension when suturing.
2. Imbricate the layers which close the defect.
3. Take care that the weak places in different layers do not overlap each other, but are covered quite reliably by other layers.

II. THE IMPORTANCE AND THE MEANS OF RELIEVING TENSION

The avoidance of all tension and stretching of tissues when uniting them with sutures is the first rule for the radical cure of hernias; without this one cannot hope for permanent results. Keeping this rule is the principal condition for the strong and permanent union of the structures which are united by the sutures.

There is a general false belief that the different structures united during the operation are held together by the sutures. Whereas this may be true for a short time after the operation, the permanency of the condition created by the operation is ensured only by the scar tissue which firmly unites the structures which were sutured to each other. This scar formation surely takes time, and the sutures must keep the united structures in contact while this occurs. If the sutures are torn or become too loose before strong adhesions between the united structures are formed, disunion of the suture line and recurrence may result. However, it should be realized that, even if the sutures are not resorbed and not torn or the knots untied, they do not constantly keep the tissues as tightly together as they did immediately after the operation, because they cut through. The greater the pressure they exert on the tissues, the earlier and the more likely will this occur, because the greater will be the extension of the aseptic necrosis which every stitch produces in the living tissue. Therefore, the greater the stress when tying a suture, the greater the probability of its early loosening or complete cutting through, even under perfectly aseptic conditions. Thus, care must be exercised to avoid too great tension upon tissues, too much when uniting them, and too great force when tying the sutures.

The stretching of the tissues and the pulling of the sutures can be avoided only if there is no tension, when the structures which should be united can be brought easily into contact with each other. This is desirable for the broad contact of the tissues which must be coaptated. This is a very important safeguard for the security and permanency of the cure. It not only prevents the loosening of the sutures, but it also eliminates the bad consequences of such an occurrence and ensures a broad and firm adhesion of the structures which were brought into contact by the operation. This is of particular importance when fascias or aponeuroses are to be sutured. They are not only very thin, but also have a very scanty blood supply and therefore the approximation of their edges with each other or with any other structure results in a thin and weak scar. Only the coaptation of broad surfaces may produce a reliable union. This can be done by mattress sutures or simple sutures, which fasten one margin of the wound to the surface of the aponeurosis at some distance from the other margin of the wound (Fig. 1).

The degree of tension in different cases and types of hernias is dependent on various factors:

1. The general condition; i.e., the tenseness or flabbiness of the abdominal wall. The flaccid abdomen of a woman who has had several children often allows easy closure of such defects which would present great difficulties if the patient were a man or a young girl.
2. The localization of the defect. Defects of large size present generally much greater difficulties if they are localized in the epigastrium

than anywhere else. This is caused by the insertion of the broad abdominal muscles on the ribs. These are very near the epigastric defects and hinder the stretching of the aponeurotic structures of this region, which consist only of the tendons of the external and internal oblique and the transverse muscles.

3. Individual conditions depending chiefly upon the size and the form of the defect and the character of its surroundings.

a. Other things being equal, the larger the defect, the greater the tension, but other factors are generally of more importance and if these are favorable very large defects often can be closed very easily and without any stretching.

b. The form of the defect is of importance in deciding upon the technique of closure because the tension of the tissues varies in different directions and by choosing the right direction for coaptating the tissues one may lessen the difficulties considerably.

c. The condition of the tissues surrounding the defect may influence their usefulness as plastic material as well as the possibility of their mobilization which may be required to overcome tension.

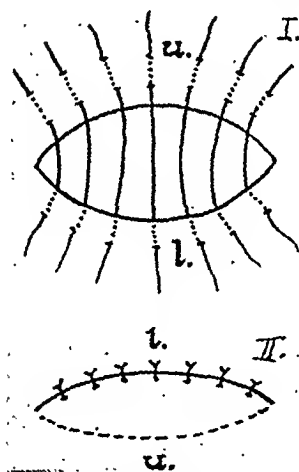


Fig. 1.—Duplication of the aponeurosis. *u*, Upper margin of the wound of the aponeurosis; *l*, lower margin; after tying the sutures the upper margin is covered by the lower one. *I*, Sutures put in; *II*, sutures tied.

III. MEANS OF OVERCOMING TENSION

This can be done principally in two ways: (1) by satisfactory mobilization of the tissues and (2) by choosing the correct method for their coaptation.

Because the latter may save unnecessary dissection and waste of tissue, it may be considered first. Different tissues bear different degrees of stress. There are also differences in the tissues which may be used for closing hernial defects, depending upon different types of hernias. There are also individual differences in the same kinds of hernias. These may be very conspicuous, especially in recurrent hernias and in

incisional hernias which all develop in postoperative scars and may therefore require individual measures.

But there are also some general rules related to the forms of the defects and these should be discussed now because they are founded on purely geometrical and physical considerations.

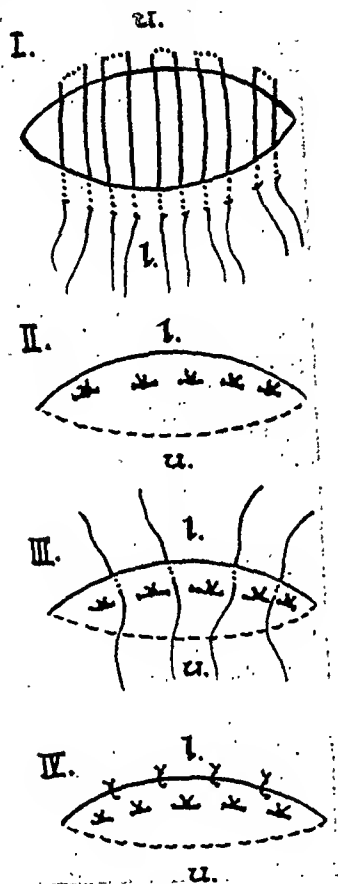


Fig. 2.

Fig. 2.—Duplication of the aponeurosis when there is a longitudinal defect with acute angles. *u*, Upper margin of the wound; *l*, lower. The duplication of the linea alba is performed in the same way; then the margins of the wound lie naturally to the right and the left. *I*, Putting in the mattress sutures; *II*, after tying the mattress sutures the upper margin of the wound is covered by the lower (so may, for instance, the left by the right one); *III*, putting in simple sutures in the free margin; *IV*, tying the second row of sutures.

Fig. 3.—*I*, Widening of a little hole of the abdominal wall; the arrows show the direction of the least resistance of the tissue surrounding the widened hole; *II*:*P*, purse-string suture; *M*, mattress suture.

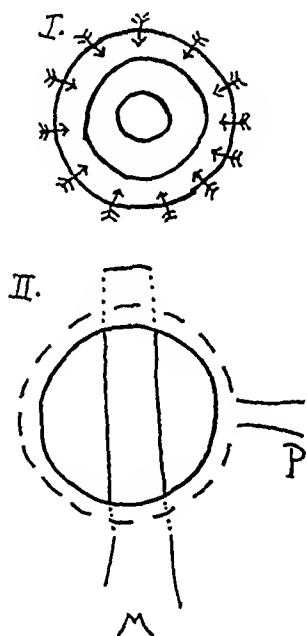


Fig. 3.

In the case in which there is a more or less linear defect, i.e., a simple slit or a relatively narrow gap whose length is much greater than its breadth and whose margins meet at more or less acute angles, the defect can be closed in the easiest way by drawing its margins together perpendicularly to the longitudinal axis of the defect. In this manner the margins meet in a more or less straight line. It is still better if

the tissues in the neighborhood of the defect are overlapped in the same direction (Fig. 2).

If, however, the defect is round, or somewhat circular, the attempt to unite its margins in the aforementioned linear manner would be the most difficult way of doing it. The opposite points would be drawn together in the direction of the chord, those in the middle of the defect in the direction of the diameter (Fig. 3-II, *M*), which is the longest chord and the greatest possible distance between any two points of the circle; but also the parts which lie at the sides of the circular defect can be united only with the greatest difficulty if a linear union is attempted. The correct method of closing these defects is based upon a consideration of their development. It is generally quite a small hole through which a small nerve or blood vessel passes, which gradually widens to a large round defect. This type of defect is encountered chiefly in umbilical or paraumbilical and in epigastric hernias,

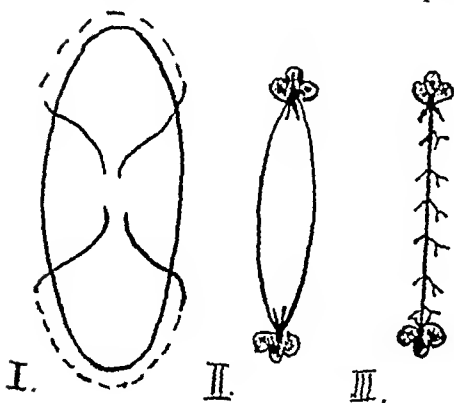


Fig. 4.

Fig. 4.—Elliptical defect. *I*, Putting in the half purse-string sutures; *II*, tying the half purse-string sutures; the defect is now slitlike; *III*, linear union of the transverse defect.

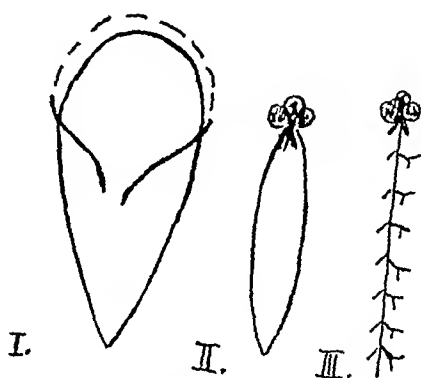


Fig. 5.

Fig. 5.—Leaflike defect. *I*, Putting in the half purse-string suture; *II*, and *III*, same as *II* and *IV* in Fig. 4.

rarely in others. When the small defect widens to a large one, the tissues bordering it are pushed always farther and farther from the center of the defect (Fig. 3-*I*). The easiest way to close such defects is to bring the tissues together by the same route they used when they were distended, because they are the most relaxed in this direction. Therefore, when closing a circular defect, an attempt should be made to bring the surrounding tissues together in the center of the circle; this is best done by a purse-string suture (Fig. 3-II, *P*). For this reason all defects which are round are closed most easily and with the least amount of tension by purse-string sutures. This cannot be done in cases in which the round defect is very small and in which its surroundings are tough, which is generally the case in epigastric hernias.

There are defects which are neither linear nor round, but elliptic (Fig. 4), egg-shaped or leaflike (Fig. 5). They may be markedly rounded on both ends or relatively long with one rounded and one tapering end. These can be transformed easily into linear ones by making a half purse-string suture on the rounded end or ends (Figs. 4 and 5). Another method to transform rounded, elliptic, egg-shaped, or leaflike defects into linear ones is to exercise the round end or ends. If they are quite small, the margins may be entirely excised so as to permit the lines of incision to meet at acute angles, or a straight incision may be made through them dissecting somewhat the edges of this incision. The latter is advisable in epigastric hernias. In other cases the half purse-string sutures are to be preferred, because they can be done much faster and easier and because tissues which are valuable as plastic material can be saved in this way and also because the closure is generally stronger.

Although the chief purpose of mobilization of the margins of the defect is to bring them into contact, it must often go much farther than this. It must provide that the tissues used for covering the defect should be resistant enough and have vitality enough to produce, when brought into contact, a strong and reliable union of the tissues in the desirable situation.

Now scar tissue cannot be depended upon to do this and therefore must often be thoroughly excised. Atrophic muscles or thin and soft fascial structures are also not suitable for the reliable closure of the hernial defects. Under these circumstances it is frequently necessary to extend the dissection far from the defect to insure the broad contact of reliable tissues.

This is generally possible and in the great majority of cases even easy. Occasionally, however, there are great difficulties, especially in cases in which previous operations have destroyed extensively the tissues surrounding the defect and it is of greater significance when suppurations and necroses follow them. In such cases flaps out of the neighborhood or freely transplanted fascial or aponeurotic grafts must be used for the covering of the defect, or at least for supporting the layers covering it.

IV. WEAK AREAS AND METHODS OF ELIMINATING THEM

There are three kinds of weak areas which threaten the permanency of cure after an operation for hernia: (1) weak areas which always must be left behind in certain kinds of hernias to give room for important anatomical structures, such as the spermatic cord, the femoral vein and artery; (2) defects which are strictly individual, for instance congenital or acquired defects of the external oblique aponeurosis in certain inguinal hernias or conditions, which, although frequent, show great individual variations as, for instance, the weakness or atrophy of the lowest portion of the internal oblique and transverse muscles in

inguinal hernias;^o (3) the suture lines and the suture perforation canals.

During the course of healing, there is always the possibility that one or more of the stitches may become untied or torn or at least somewhat loosened and, owing to a sudden increase in the intra-abdominal pressure, the whole suture line or part of it may separate. Not only during the healing but even after the formation of the scar, the suture line always presents a weak area, particularly when the edges of the structures are linear, which means that their surfaces of contact are quite narrow. Scars are rigid because they do not contain elastic fibers but only connective tissue; they may withstand pressure, but if they are once stretched by it, as emphasized long ago by Girard, they cannot return to their former size. If this pressure is often repeated, as always occurs in the abdomen because of coughing, sneezing, pressing at defecation, urinating, etc., the scar will be permanently dilated, and with the lapse of time it will become more dilated. It will always become broader and thinner, especially if there is only one scar connecting peritoneum and skin, as occurred, for instance, if all the layers of the abdomen from the peritoneum to the skin were united by

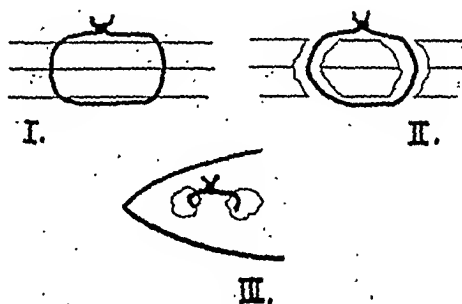


Fig. 6.—How the suture cuts through. *I*, Suture freshly put in; *II*, after cutting through (cross section); *III*, the defects caused by this from above.

through-and-through stitches as was often done a few decades ago, especially after laparotomies in the midline. It may also result when the scars uniting the suture lines of the different layers of the abdominal wall cover each other geometrically; i.e., lie in the same plane; or else when there is a suppuration which makes the open treatment of the abdominal wound going from the skin to the peritoneum necessary.

In all these cases one must reckon with the gradual distention, weakness, and enlargement of the scar which results in hernia or, if the operation is done for hernia, in the recurrence of the hernia.

Not only the suture line itself but also every stitch may cause hernia or the recurrence of the hernia if they connect the preperitoneal and subcutaneous fat. This occurs for example in the Mayo operation for umbilical hernia in which the sutures go through both layers of the aponeurosis covering the defect. Every stitch causes, as already mentioned, an aseptic necrosis, cuts through and produces, in this way,

defects (Fig. 6), which may be filled more or less with scar tissue, which is likely to distend. Moreover, sometimes even before the scar has formed, some peritoneal fat may protrude into the hole which will gradually widen later.

How are these weak spots to be eliminated? (1) By multiplication of the layers, (2) by covering the weak spots with fully reliable resistant tissue, and (3) by carefully avoiding weak areas to be situated so that one lies directly over the other.

If, for instance, the spermatic cord is directed by the shortest route through the abdominal wall, it would pass through all layers at the same vertical plane and this would predispose to recurrence; but, if it is directed through each layer in a different vertical plane, this cause of recurrence is eliminated. Therefore we must separate the weak places and put them as far from each other as possible. This rule must be strictly followed when arranging the suture lines. One must try to put them in a way that no suture line should lie directly below or above the other, that every suture line should be covered with a completely intact layer of tissue, and, if possible also, that the suture lines of the different layers should lie in different directions.

Such a situation of the suture lines diminishes very considerably the dangers presented by the intra-abdominal pressure and especially its sudden increase. It safeguards the suture lines and the scars resulting from them (1) by diminishing the strain to which they are exposed; each suture line protects the other if they are situated as described before. (2) Should some separation of a suture line or some enlargement or weakening of a scar occur, the covering or underlying resistant layer of tissue hinders the development of broader gaps and hinders certainly the protrusion of the underlying structures and in this way eliminates the possibility of recurrence.

V. ADDITIONAL REMARKS

1. No operation starts and ends in the operating room; the preparation and after treatment are of equal importance. After the operation for hernia, the patient should be carefully guarded against any greater increase of abdominal pressure. This is very important for the integrity of the sutures; therefore, one must take care that bronchitis, pneumonia, vomiting, and difficulties in defecation and urination are avoided.

2. The material used for suture must be resistant enough to keep the sutured parts in place at least for one or two weeks.

3. The difficulties of the hernia operation are very different in different cases. There may be difficulties either in eliminating tension or in providing useful tissues for the reliable covering of the defect or in both. Some difficulties may be overcome by favorable anatomical conditions, in such a way that often very large hernial defects can be closed with astonishing facility; whereas, in other cases these diffi-

culties only allow a rather unsatisfactory closure of relatively small defects.

One must never forget that every operation for hernia is a plastic operation and that like other plastic operations the individual peculiarities of the case must always be duly regarded. This is true also for the so-called typical cases but chiefly for recurrent cases and incisional hernias where the normal anatomical conditions are greatly disturbed and often also normal tissues replaced by masses of scar. The more prominent these anatomical changes, the greater is the difficulty of following the rules made for typical cases and the greater the necessity for individualizing.

In the following paragraphs the methods which I have used and which have been used by my assistants, most of them for more than thirty years, are described. They were published in Hungarian, some of them also in German, but they are unknown in America.

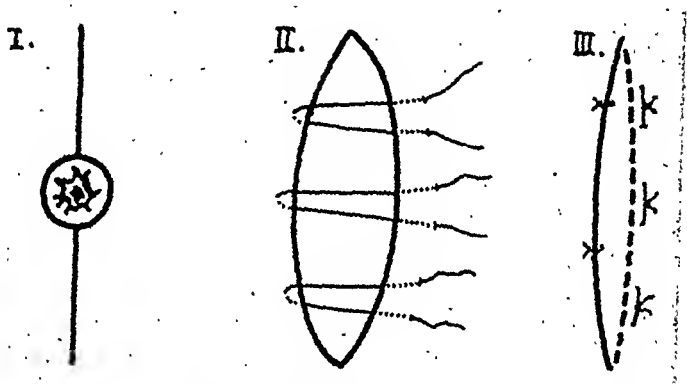


Fig. 7.—Epigastric hernia. I. The hole of the linea alba halved by the incision; II, mattress stitches; III, second row, simple stitches.

VI. EPIGASTRIC HERNIA

Epigastric hernias are generally very small, mostly not larger than a pea or a hazelnut, and the linea alba through which they protrude is generally very rigid; therefore the defect cannot be closed by simple suturing and even less by the duplication of its margins. Besides, the defect is so small that only one single suture could be used and this only at the diameter of the defect which is in the direction of the greatest strain. Therefore it is not secure even if made in the manner of the Lembert sutures as advised by Witzel (Fig. 1).

It is better to transform the small round defect into a long linear one by making an incision 4 to 5 cm. in length in the linea alba, which halves the defect. After retracting the margins of this incision, three sutures are placed, as shown in Fig. 2. It is preferable to use a suture with two curved needles; one needle is inserted through one side of the aponeurotic wound about 1.5 cm. from its margin and then both

needles are inserted through the other edge of the aponeurosis from the inside stitches; one side of the aponeurosis is drawn below the other and now the free side of the above lying one is sutured to the aponeurosis which lies below (Fig. 7-III). In this manner the linea alba is duplicated. It is generally sufficient to use three mattress sutures and two superficial simple ones, which are best placed in the intervals between the mattress sutures.

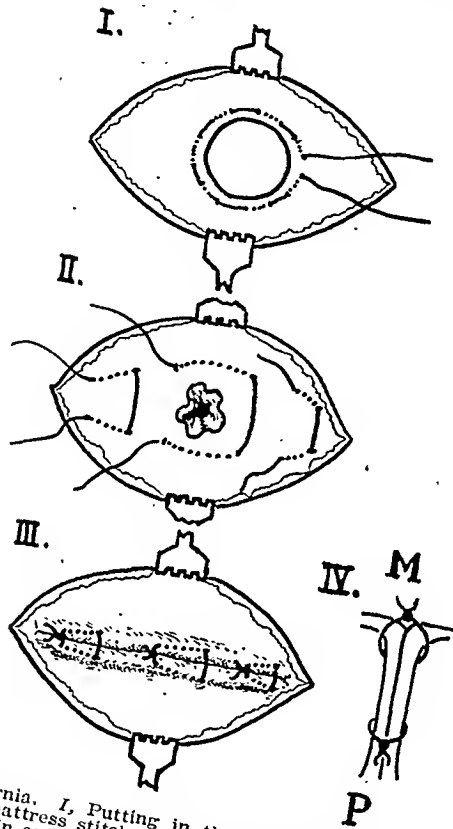


Fig. 8.—Umbilical hernia. I, Putting in the purse-string suture; II, purse-string suture tied, transverse mattress stitches put in; III, mattress stitches tied; N, purse-string suture; P, tucked in and covered by the mattress suture; M, cross section.

This method was first published in 1908¹ and has always given excellent results. Larger epigastric hernias are very rare, but in these the laxity of the surrounding tissues permits their closure with purse-string suture, as will be described for the umbilical hernia.

VII. UMBILICAL HERNIA

After the excision of the sac, the defect of the umbilical hernia is generally round. One must economize with the fascia, which is generally adherent to the peritoneum, and utilize as much of it as possible. After the replacement of the abdominal contents, a strong purse-string suture is installed which goes through fascia and peritoneum; the suture is placed about 2 cm. below and 2 cm. above the tissue formed by aponeurosis and peritoneum and about 1 to 2 cm. from its edge. Some-

what larger bites of tissue may be included in one stitch if the defect is larger and correspondingly less in smaller ones. The beginning of the thread is left long and the end one is brought out at the surface about 2 cm. from the former. The ends of the thread are pulled taut and tied. It is surprising how large openings can be closed with a single purse-string suture (Fig. 8-I).

This purse-string suture must be covered, preferably by two or three mattress sutures, which are placed through the aponeurosis so as to bring the soft parts together over it at right angles to the long axis of the body (Fig. 8-II), as advised also by Rotter (Fig. 8-III, IV). Closure by approximation of the rectus muscle and its aponeurosis after incising the rectus sheath as advised by Maydl is superfluous. I did this in my earlier cases and advised first the purse-string suture as a trick facilitating Maydl's operation,² but I discontinued this many years ago and do it only in very exceptional cases. We have obtained very good results with the closure of the defect by purse-string suture and by covering these with simple horizontal folds of the aponeurosis fixed by a few mattress sutures.³

VIII. INCISIONAL HERNIAS

In incisional hernias one must try not only to re-establish the normal anatomical structure of the abdominal wall but also to reinforce it as much as possible. The reinforcement of the linea alba can generally be accomplished in quite a typical way; whereas, other cases require a great variety of techniques, depending upon the site and size of the hernia, the kind of incision which was made at the former operation, the amount of scar tissue and the plastic material, etc. The difficulties cannot be realized until the anatomical situation is apparent, and this cannot be determined before the hernial sac, which often overlaps the margins of the defect and may protrude for a considerable distance between skin and aponeurosis, is clearly dissected and excised. The size and form of the defect become apparent only after the replacement of the abdominal contents and the closure of the hernial sac. One can then decide upon the best method of closure.

Median Hernias.—If there is a longitudinal defect which is relatively narrow and tapering at both ends and if the margins are readily mobile or can be made so by undermining, the best method consists of drawing one edge of the defect below the other with mattress sutures and stitching the margin of the overlying side to the aponeurosis which is below. One may use sutures with needles at both ends and place the suture as previously described and as shown in Fig. 7. The two needles are passed through the tissue at a distance 1 to 1.5 cm. apart. The space between the two sutures should be about 1.5 to 2 cm. It is advisable to put in all the sutures before tying them. The tension, which is generally greatest in the middle, is diminished remarkably. After all the mattress sutures are tied and the sides of the defect overlap each other for 1 to 4 cm., the free margin of the overlying side is sutured to the underlying

aponeurosis with interrupted sutures, preferably placing them between the mattress sutures (Fig. 2-III). If there is a broad defect with rounded ends, or at least one of the ends is rounded, one must first transform it into a defect with pointed ends by the half purse-string suture (Figs. 4 and 5). This will also simultaneously reduce the length of the gap which can now be united with interrupted sutures (simple or mattress sutures). However, it is generally impossible to produce a broad enough duplication; therefore, it is usually advisable to cover this suture as well as the half purse-string sutures by splitting the rectus

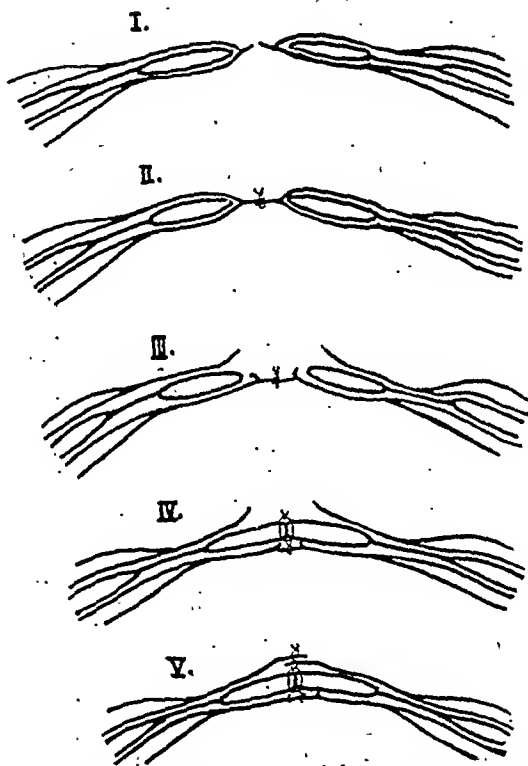


Fig. 9.—Incisional hernia. *I*, Defect of the linea alba; *II*, united; *III*, medial part of anterior rectus sheath opened; *N*, rectus muscles united; *V*, anterior rectus sheath duplicated (cross section). The suture of the medial wound of the rectus sheath (posterior rectus sheath suture) is not illustrated, but it should be done.

sheaths, which were brought close together by the former suture, as near the median line as possible, and sew them together with interrupted mattress sutures. The rectus muscles are then approximated and their anterior sheaths are sutured (Fig. 9). This is not very difficult, especially in multiparous women, and is even easier below the umbilicus. Even in men, defects below the umbilicus can be repaired in most cases relatively easily, but in the epigastric region this often cannot be done as reliably as desired. It is particularly important to approximate the edges of the anterior rectus sheaths because most of these patients are heavy smokers and frequently have bronchitic complications and consequent coughing with resultant tension on the su-

tures. Therefore, in such cases a large flap from the fascia lata covering the rectus muscles and bridging the gap of the rectus sheath is often advisable.

Lateral Hernias.—The great variety of the anatomical conditions in lateral hernias does not allow the description of a typical technique. Nevertheless, certain useful general rules may be observed: (1) Conserve any tissue which may be useful for covering the defect. (2) Expose carefully all normal structures which surround the defect. This generally mobilizes them satisfactorily. If it does not, further mobilization must be done very carefully, sparing aponeuroses, muscles, nerves, and blood vessels as thoroughly as possible. (3) Reconstruct as far as possible the normal anatomical conditions, doubling at least the aponeuroses, especially the aponeurosis of the external oblique muscle, which is very often conspicuously distended. (4) Make the incision of the rectus sheath near its lateral border; the mobilization of the rectus muscle helps in many cases to close the defects or at least to multiply the covering layers. (5) If the hernia developed in a defect of the rectus muscle itself, so that the hernial defect involves the posterior rectus sheath, its doubling or closure or at least the reduction of the size of the defect and the transformation of its form, by purse-string or half purse-string sutures, may considerably reduce the difficulties of the closure. (6) In cases in which the nerves of the rectus muscle, or at least those of its median portion, have been severed, which occurs in practically all cases in which a longitudinal incision has been made through the rectus muscle or lateral to it, the paralysis of the rectus muscle or at least of its medial part must be assumed; this condition is likely to promote recurrence if the anterior sheath is not reliably reconstructed. Therefore, in such cases the careful union and, if possible, duplication of the anterior rectus sheath or even a fascia lata graft are advisable.

IX. INGUINAL HERNIA

The general principles of the radical closure of hernial defects of the abdominal wall discussed in the first four paragraphs can be realized in the most ideal manner in the overwhelming majority of inguinal hernias, but there are certainly exceptions; namely, some recurrent hernias and some direct hernias.

Recurrent hernias present difficulties chiefly in patients who have been operated upon several times or who have had previous suppuration. As a result of these factors, very valuable plastic material gets lost. For example, the aponeurosis of the external oblique muscle may become defective or shrunken and the muscles surrounding the inguinal canal may be replaced by hard callous scar tissue. In such extreme cases free grafting of fascia or flaps from the neighborhood* may be necessary, but in most cases one may ensure quite reliable covering by ample mobilization of the rectus muscle. The failing aponeurosis of the external oblique

*In one of my cases the defect was covered by a flap consisting of skin, fascia lata, and sartorius.⁵

muscle may be replaced sometimes by a broad continuous layer of resistant scar tissue. This is a very incomplete substitution, but better than nothing and although not as valuable is simpler than the graft of fascia lata.

The reliable closure of the hernial defect may be difficult in cases of direct hernias when the internal oblique and transversus muscles are poorly developed. This occurs frequently, especially in people whose entire abdominal musculature is very weak. Not infrequently it occurs in people with good musculature. Defects of the aponeurosis of the external oblique muscle may also hinder the usual closure of the hernial defect; and, if both conditions are present, they may make the reliable covering of the hernia doubtful. But this happens extremely seldom indeed and in most cases the aponeurosis of the external obliquus muscle is so well developed (in large hernias) that it may be largely substituted for the weakened lowest part of the internal oblique and transversal muscles. There is perhaps no other operation in the whole surgical literature which has been as often modified as the widely adopted method of Bassini for inguinal hernia. I too committed this sin thirty-six years ago,⁴ but I never had cause to repent it. The method I advised is a combination of the modifications described by Halsted, Berger, and Girard and completed by a few small tricks of my own. It gives excellent results. Many thousands of inguinal hernias were operated upon by this method with practically no recurrences. The very few cases of recurrences which were observed occurred only in cases in which there was suppuration or in which the operation was done for a recurrent hernia.

A broad flap of the aponeurosis of the external obliquus muscle must be prepared with its incision at the upper angle of the subcutaneous opening of the inguinal canal. The incision should be made parallel with the fibers of the aponeurosis and end about 3 to 4 cm. lateral to the abdominal opening. After dissecting the flap, this is drawn downwards and the hernial sac treated adequately. After its replacement the spermatic chord is exposed and if too voluminous some of its veins and the cremaster are resected.

The next step consists of incision of the rectus sheath (Fig. 10-1) which may be unnecessary in cases in which the lower part of the internal oblique and transversalis muscles are very well developed. This occurs frequently in congenital hernias of children or young men with strong musculature but very seldom in other cases. In those with poorly developed musculature the rectus sheath must be opened to such an extent that the upper end of the incision should reach the site of the well-developed part of the internal oblique and transverse muscles or slightly beyond it. The length of the incision should be about 5 to 6 cm. in the adult. The rectus muscle and the external margin of the incised rectus sheath as well as the internal oblique and transverse muscles are sutured to Poupart's ligament (Fig. 10-2, 3). Care should be exercised that the suture should include the well-developed part of the latter muscles.

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stitches about at the junction of the medial and middle third of Poupart's ligament (Fig. 10-5).

By this method the inguinal defect (the weak area between Poupart's ligament, lateral side of the rectus, and lower border of the well-developed parts of the internal oblique and transverse muscles) is covered by three reliable layers (one muscular and two aponeurotic) and the weak areas resulting from the passage of the cord are eliminated. The internal abdominal ring is reliably covered with the above-mentioned three layers; the cord itself passes outward at least 2 to 3 cm.

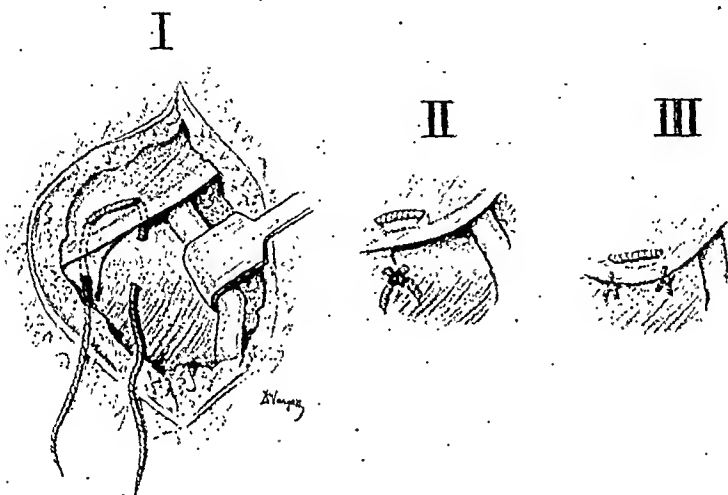


Fig. 11.—Femoral hernia. *I*, Mattress stitch put in through Poupart's and Gimbernat's ligaments and periosteum of the pecten pubis (ligamentum Cooperi); *II*, mattress stitch knotted; *III*, Poupart's ligament sutured to the fascia of the pectineus muscle.

in a narrow museuloaponeurotic canal and, when it reaches the external surface of the lower aponeurotic flap, it is kinked in an acute angle and lies then in a narrow aponeurotic canal and comes out of it through a small transversal opening, between two stitches. Behind it lies a strong aponeurosis.

If the rectus sheath is not opened or even if that is done, the inguinal canal may be closed also (of course, only after the suture of the muscles to Poupart's ligament is completed) by attaching the upper margin of the incised aponeurosis of the external oblique to Poupart's ligament, displacing the spermatic cord as far as possible laterally, and, after kinking it in an acute angle (Fig. 10-6), covering it with the lower flap of the aponeurosis (Fig. 10-F).

This also gives excellent results because it covers the muscles and the suture uniting the muscles with Poupart's ligament reliably and ensures the angulation of the spermatic cord in a perfect manner. Moreover the most medial part of the suture, where recurrences most frequently occur, is well protected.

During this stage of the operation, the spermatic chord must be retracted as far laterally as possible and fixed in this position by the most lateral sutures which unite the broad muscles with Poupart's ligament.

The most medial suture should include the whole thickness of Poupart's ligament and the lateral crus of the subcutaneous inguinal opening. Thus for this suture whose knot lies in the deepest layer of the subcutaneous fat I generally use nonabsorbable material (silk);

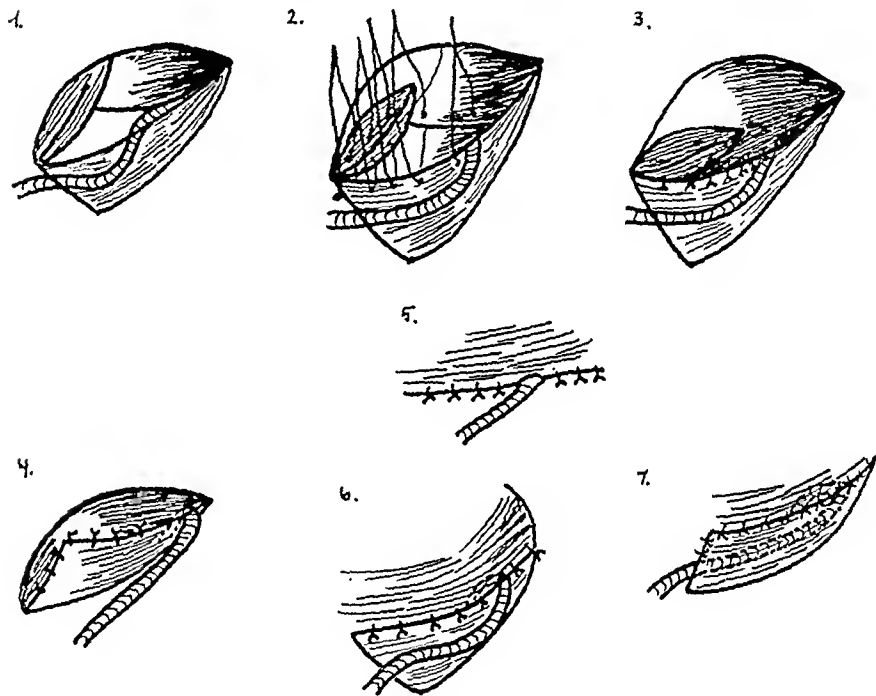


Fig. 10.—Inguinal hernia. 1, The inguinal defect; 2, lower flap of the aponeurosis of the external oblique put downward, incision of rectus sheath; 3, deep sutures put in; 4, tied; 5, lower aponeurosis flap sutured (mark angulation of the cord); 6, upper aponeurosis flap pulled down and sutured; 7, upper aponeurosis flap sewed to Poupart's ligament (mark angulation of the chord); 8, lower aponeurosis flap sutured to aponeurosis.

whereas, for all the other internal sutures and ligatures, I use catgut. This most medial stitch is exposed to the greatest stress, therefore it is best to tie it last.

The margin of the lower flap of the external oblique aponeurosis is sutured first to the medial margin of the incised rectus sheath (Fig. 10-4). The rest of this aponeurosis flap is sewed as far as possible to the internal oblique muscle. The transplantation of the spermatic cord outward is continued (Fig. 10-4). When the last suture which lies close to the spermatic cord is tied, the cord is placed on the external surface of the lower flap of the aponeurosis and the upper margin of the incision of the aponeurosis of the external oblique is sewed to Poupart's ligament. The spermatic cord is led out between two

OSTEOMYELITIS OF THE JAWS*

AN ANALYSIS OF FIFTY-NINE PATIENTS

EARL C. PADGETT, M.D., KANSAS CITY, MO.

(From the Surgical Department of the University of Kansas School of Medicine and the Kansas City Western Dental College)

THE influence of the teeth and tooth buds on the course of infection of the jaw bones in contrast with the other bones of the body lends a unique interest to osteomyelitis of the jaws. The danger of initiating a severe infection of the jaws, when he uses bad judgment in regard to the optimum time to inflict operative trauma, is a threat which often hangs over the head of the exodontist. In this paper I wish to discuss generally what one might term "frank" osteomyelitis from the standpoint of my own material during the past ten years. In the group are fifty-nine patients. The cases of osteomyelitis following fracture have been excluded from the group. As a matter of fact, in both the acute and chronic alveolar abscess an osteomyelitis is present, but it is not common practice to use the term osteomyelitis in describing these lesions.

In the group are two unique examples of a type of slowly progressive osteomyelitis of the upper jaw which extended to the skull, producing death eventually because of a meningitis. I wish to suggest that these two patients are possibly examples of a more or less unique clinical entity on which little stress has been placed previously.

The maxim to be drawn from a study of the pyogenic group as a whole is that, as a rule, treatment during the acute stage should be conservative, but on the contrary, after sequestration has been effected, fairly thorough and somewhat radical treatment is the most effective.

INCIDENCE

Frank osteomyelitis of the jaw bones is not very common. Leibold considers it eighth in frequency. The femur, tibia, humerus, radius, ulna, vertebrae, and os calcis precede the mandible in the order named. Wilensky in the Mt. Sinai series (1924-1930) found 450 patients with acute and chronic osteomyelitis of all kinds. The upper and lower jaws were involved in 39 instances.

In my series of 59 patients, 22 were below the age of 16 years and 37 were older; 21 cases occurred in the female and 38 in the male sex. The mandible alone was affected 38 times and the maxilla alone 16 times and in 3 patients both the mandible and the maxilla were involved. One of these was an osteomyelitis due to excessive irradiation and the other two were of the pyogenic type. In 2 other patients with a slowly progressive osteomyelitis of the maxilla the inflammatory

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X. FEMORAL HERNIAS

The difficulty of the radical operation for femoral hernias is the avoidance of compression of the femoral vein. Therefore, a forced closure of the hernial opening is not only impossible, but even undesirable. If Poupart's ligament is used for the closure and forcibly brought down and attached to the periosteum of the os pubis, one may enlarge the inguinal canal and have an inguinal recurrence. The inguinal route has its own drawbacks (especially when there is a strangulated hernia) and does not exclude with certainty the above-mentioned disadvantages and makes even good partial closure of the crural canal difficult. One must rely on the high ligature of the sac and that is generally not enough. For large crural hernias, especially those that are recurrent, the neighboring muscles may be used. I described, many years ago, the implantation of the sartorius muscle in the crural canal, but I perform this operation only in very exceptional cases. The splitting of the rectus sheath and uniting of the rectus with the perios of the os pubis and the covering of this with a flap of fascia lata is easier and ensures pretty good closure. But in small hernias even this is too much, so I generally put a mattress suture 1 to 1.5 cm. over Poupart's ligament in the aponeurosis of the external oblique. The medial part of this suture also passes through Gimbernat's ligament (Fig. 11-I) and then both threads go through the periosteum of the os pubis. The lateral suture is placed as near the femoral vein as possible without compressing it. After this mattress suture is tied, Poupart's ligament is sewed with a few stitches to the fascia of the pectineus muscle (Fig. 11-III). This is somewhat stronger than the similar method of Kocher, Payr, etc., but there is really no absolutely reliable method for curing femoral hernia and one must in these cases be more prepared for recurrences than in any other form of hernia, except those incisional hernias which lie in the median line above the umbilicus, especially when the patients are men and the hernias large.

Ultra posse nemo tenetur. One cannot cure everything, but one must try to do one's best, which means in hernias, multiply the layers and cover the weak areas as reliably as possible under the given anatomical conditions.

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possibly the dentists at the present time do not so often extract a tooth during the acute stage. In Blair's 39 cases, published in 1923 and 1926, wherein he emphasized particularly the dangers of extracting the ulcerated tooth during an acute stage, 31 were associated with extraction of a tooth during the acute stage. The number of cases (9) due to syphilis in our series is rather high. Most of these individuals were referred to me because a reconstruction operation would be necessary eventually. Osteomyelitis due to excessive irradiation in the older series of published cases is not listed. However, today it is not uncommon to have an extensive osteomyelitis due to a secondarily infected bone irritated by excessive irradiation. Although no cases of slight adjacent necrosis purely due to the local effect of the implantation of radium were included, in the series were found 6 cases with necrosis of the complete thickness of the mandible after excessive irradiation.

ORGANISMS

Rosenow, Gilmer, and Moody and Haden present evidence to show that the common organism associated with a periodontal infection is the *Streptococcus hemolyticus*. Less commonly the staphylococcus or a mixed infection causes the infection. When osteomyelitis of the jaws is caused by a blood-borne organism, the offender is usually the *Staphylococcus aureus*. A blood-borne infection, however, occurs only rarely. When trauma or disease is the cause of a secondary infection of the jaw bone, a mixed group of organisms of the variety commonly found in the mouth usually is present.

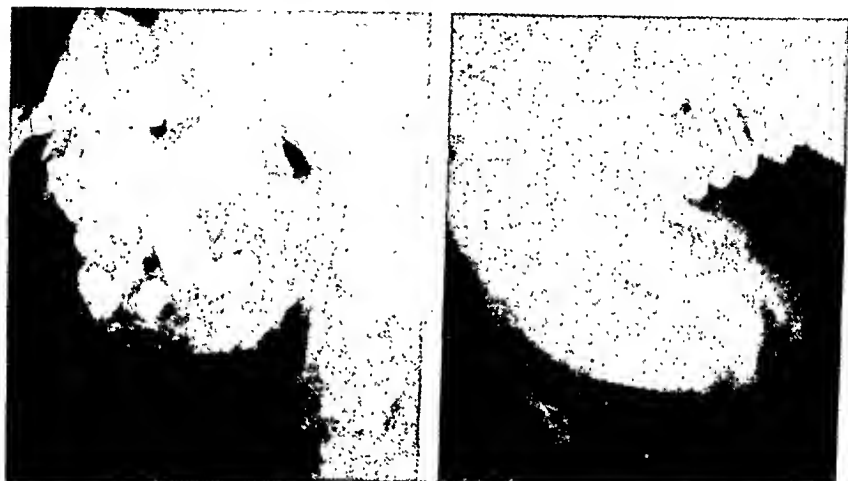
PATHOLOGY

The pathology of an osteomyelitis of the lower jaw is influenced especially by two factors: (1) the presence of dental elements in the bone and (2) a unique blood supply. The pathology of the upper jaw may be influenced particularly by four factors: (1) the presence of the dental elements, (2) a unique blood supply, (3) the fact that the bone is of membranous origin, and (4) the presence of the maxillary sinus.

Besides the preceding special factors, an osteomyelitis of the jaws shows the same pathologic changes as any other fibroblastic tissue containing a deposition of lime salts in the ground substance. Briefly, as the products of inflammation accumulate under tension, the vessels within the bony spaces become thrombosed. The bony trabeculae tend to be absorbed and the products of inflammation following the path of least resistance seek an outlet through the bony cortex. After the cortex is perforated, some elevation of the periosteum occurs before it, in turn, is perforated. The cellular reaction encountered as a sequestration takes place and involucrum is formed in the jaw bones is, on the whole, the same as that which occurs in other bones and needs little comment here, save to emphasize that a line of demarcation is formed between the live and dead bone which is usually complete in from two to three months

process also eventually involved the base of the skull and the frontal bones, although originally the process started in the maxilla.

The etiology is interesting. The disease in over one-third of the patients (25) was associated with a peridental infection. In 11 patients the disease was associated with an extraction during the acute stage of a pulpitis or a peridental infection (Fig. 1A); 12 developed from an infection of the pulp cavity unassociated with extraction and in 2 patients too much mercury was the basis of the necrosis.



A.

B.

Fig. 1.—A, This boy had a toothache August, 1933. The jaw became tender and he had some fever. The tooth was removed. He became very ill. A good many of the lower teeth became loose and dropped out. When I saw him Nov. 5, 1933, his jaw was underdeveloped. Most of the teeth and the tooth buds were absent. Here and there was some dead bone all through the mandible. The mandible was explored; all infected tooth buds were removed; all granulating sinuses were laid open; and all overhanging bone was removed. After this operation the boy was cured, but the lower jaw has not developed as much as it should.

B, Roentgenogram of boy aged 16 years. He had a blister on his foot and two days later developed an osteomyelitis of the lower jaw. He was seen by me three months later. At that time he had lost all of his teeth and tooth buds and the alveolar ridges of the lower jaw. There had been considerable new bone formation and after a moderate sequestrectomy the jaw healed. Some months later the gingivolabial sulcus was deepened and a denture fitted.

In 5 patients trauma to the jaw in the region of the tooth initiated the infection. In 4 the bone became infected after an operative extraction. In 2 of these individuals, although the tooth or root was removed, it was found that the dentist had fractured the jaw in removal. In 1 of these patients the jaw was very atrophic. In 1 patient a corrosive fluid had been injected.

In 29 patients the origin of the lesion seemed to be other than a peridental infection or trauma. Of these, 4 were of the blood-borne type (Fig. 1B); 19 were due to syphilis; 6, to excessive irradiations; 1, to noma; 1, to trauma of the cheek; 3, to leucemia; and 3 possibly originated from an infection of the maxillary sinus.

If one compares the etiology of these cases with certain other published groups, for example those of Blair, one gains the impression that

will cause trismus and swallowing will be impeded when the tissues of the floor of the mouth or pharynx are invaded. In osteomyelitis of the upper jaw the inflammatory products may extend into the tissues of the anterior cheek, nose, or palate. When the tissues of the hard palate are undermined, there may be no particular redness because of the compact structure of the soft tissues in this region.

When drainage is provided either spontaneously or by incision, the pain, swelling, and constitutional reaction largely subside, but sinuses with pouting projections of granulation tissue persist as long as dead bone or dead tooth structure remains in situ. A few cases of osteomyelitis of jaw bone result in slow bone absorption without actual gross death of bone, but as a rule a definite sequestrum is formed, which takes about two or three months to become separated from the live bone.

Often age influences the course of osteomyelitis of the jaw considerably. In nurslings the characteristic invading organism is one of great virulency and as a rule a septicemia either precedes, accompanies, or follows the infection. In children often the damage to the tooth buds which necessitates their removal may seriously interfere with the subsequent growth of the jaw bone even if the amount of sequestration does not cause serious deformities.

In the bone necrosis seen accompanying a primary blood disease, the soft tissues about the necrotic bone usually show only a slight reaction. The constitutional symptoms tend to be more severe than the local condition would lead one to suspect. The general appearance of an adult, rather pale and yellow, and the fact that no other obvious etiology seems to be present suggests to one immediately that a blood smear is advisable.

The outstanding feature of an irradiation necrosis is the chronicity of the course, the continued pain, the slowness of sequestration, lack of tendency for either the bone or the surrounding soft tissue to show any of the ordinary tendencies of normal tissue toward healing, and finally lack of resistance to secondary infection.

When a child is seen with evidence of a bone infection in the region of the epiphyseal cartilage of the condyle, rather often it is difficult to be certain whether or not one is dealing with a purulent arthritis of the temporomandibular joint or a true blood-borne osteomyelitis of the type more commonly seen in the other long bones. The region in front of the ear is swollen and tender and in either case great difficulty is experienced in moving the lower jaw. The joint cannot be aspirated well. The only possible distinguishing signs are that the swelling and point of maximum tenderness should be lower in an osteomyelitis and less difficulty should be experienced in moving the lower jaw.

LOCATION AND SIZE OF SEQUESTRUM

Classification as to the location and the size of the sequestration is of some interest. This in our series was as follows: In the body of the

and that as long as any dead bone is present the opening in the periosteum will persist through which pus and debris will drain. It is to be remembered that the maxilla is a membranous bone and therefore it lays down little or no new bone. The products of inflammation about a tooth cause the fibrillar connections between the periodontal membrane and the cementum of the tooth to be disrupted. The cementum once denuded remains denuded. The cementum has no blood supply and does not exfoliate. As long as the tooth is present, the uncovered cementum acts as a nonviable, irritating foreign body. Before the teeth are erupted the dental sacs may be involved in the inflammatory process; when this occurs, the unerupted tooth or teeth become isolated, nonviable, and act as foreign bodies in a manner similar to a sequestrum.

The amount of devascularization of the bone depends upon the degree of stripping of the periosteum on the one hand and the degree of central thrombosis on the other. Thus, if sufficient periosteum is stripped from either bone of the jaw while coincidentally the central blood supply is blocked, complete necrosis of the whole bone may ensue. This is especially true of the mandible where the centrally located inferior dental artery furnishes blood to the central part of the bone.

The blood supply of the upper jaw is also somewhat unique. Wilensky recently has emphasized that the upper jaw receives the blood supply principally from two arterial branches, the anterior dental which passes in front of and the posterior dental which passes behind the antrum to anastomose with each other in the superior alveolus. As the blood supplied by the periosteum to the maxilla is quite meager, the size of the sequestration is particularly influenced by the location of the thrombus and the amount of thrombosis that may be present. In the type of osteomyelitis that may occasionally occur in nurslings, this may be particularly true.

CLINICAL COURSE

The outstanding early local symptoms of an osteomyelitis of the jaw, as in osteomyelitis elsewhere in the body, are severe, aching, throbbing, deep-seated pain, or in the recumbent position a developing local tenderness, worse on percussion, and local swelling which eventually fluctuates if the tension within is not too great. The general symptoms are those which accompany any pyogenic infection. As a rule as soon as the periosteum is perforated the pain decreases, but, if the pus is evacuated in the soft tissues about the bone, the swelling tends to increase rapidly. The location of the main infection and the direction the products of inflammation take as they enter the soft tissues influence the symptoms considerably. In involvements of the lower jaw the pus sometimes extends into the deep tissues of the submaxillary region, the upper deep cervical region, or into the tissues into the region of the anterior pillars. Involvement of the muscles of mastication

involvement of the maxillary bone, a small ulceration developed in the soft tissues anterior to the maxilla. Sloughing of the soft tissues and necrosis of the bone continued slowly. Both small and large sequestra formed. First, the front of the face and the nose sloughed away. Finally the invasion extended to the frontal bone and the base of the skull. In both patients the course of the disease was known to have been in the neighborhood of eighteen months before death from a meningitis.

One of the patients (Fig. 2) had a history of receiving some "shots" several years previously. The Wassermann test of each was negative. Each received intensive antisyphilitic treatment. Each had a history of antral insult, one a kick by a horse (Figs. 3 and 4) and one an antral operation. Cultures, both aerobic and anaerobic, were run on both.



Fig. 2.—Case of progressive osteomyelitis of the maxilla which started after traumatic injury to the antrum successively involving the frontal bones and base of skull, death finally resulting from a meningitis. A, Photograph taken Jan. 13, 1939; B, photograph taken Aug. 18, 1939, just before his death. (Case of Dennie.)

Biopsy specimens were taken on both and finally autopsy was performed. Each had tests for glanders leishmaniasis (N.N.N. medium and tartar emetic). The biopsy reports were consistently granulation tissue. It is known, however, that in gangrenous conditions about the face and mouth spirochetes are usually present. From one of these some spirochetes were seen, but the pathologist (H. R. Wahl) was unable to identify them as the *Spirochaeta pallida*. They were probably secondary invaders. Guinea pig inoculations were made without positive findings. One patient (Figs. 3 and 4) had been in Mexico. The

mandible alone 6 showed a small sequestrum, 13 a sequestrum of medium size, and 12 a large sequestrum but not involving a whole section of the bone. In 6 others the sequestrum was so large that the continuity of the bone was discontinued. In 1 the sequestrum was the ramus and in 1 the condyle and the neck. In the maxilla alone 2 showed a small amount of sequestration, 11 a medium amount, and 5 a large amount. In 3 patients sequestrum appeared in both mandible and maxilla. In 2, 1 following mereury and 1 following excessive irradiation, the sequestrum was of large amount. Characteristically in the necrosis due to mercurry the alveolar ridges were lost principally. In irradiation necrosis characteristically the whole thickness of the mandible becomes secondarily infected and necrotic. In the syphilitic cases the palatal process or the frontal process of the maxilla was involved most commonly. In the latter case the bone usually was involved by extension from the nasal bones.

THE ROENTGENOGRAM

Early some mottling of the bone usually is to be seen in the roentgenogram. Usually after six or seven weeks one may get some idea of the probable amount of sequestration. A hazy, moth-eaten, uneven outline between the edges of the live bone and the dead bone begins to become evident and the sequestrum shows as an irregularly shaped piece of bone lying in a cavity surrounded by either uninvolved bone or new bone. Later the sequestrum loses some of its density. In those cases in which the necrosis is the full thickness of the jaw, the roentgenogram aids in judging the extent to which the involucrum or new bone has formed. Repeated roentgenograms over a period of six to nine months may be necessary before there seems to be sufficient new bone not to jeopardize the contour of the lower face when the sequestrum is removed.

TWO PATIENTS WITH UNIQUE PROGRESSIVE OSTEOMYELITIC AND SOFT TISSUE DESTRUCTION OF UPPER JAW REGION, BASE OF SKULL, AND FRONTAL REGION*

Of unique interest are the patients with a progressive osteomyelitic and soft tissue destructive process of the upper jaw region, frontal region, and the base of the skull. In the literature an exact description of a similar clinical course has not been found. The clinical courses of these two patients were strikingly similar. The patients were both men in middle life. Previously they had been in good health. In each case the onset seemed to have been associated with antral infection and trauma (Figs. 2, 3, and 4). Accompanying and following the

*These two patients were seen in consultation. The first was a patient of Paul Stookey (Figs. 3 and 4) and the second a patient of Charles Dennie (Fig. 2), of Kansas City. It is with their consent that I publish them. The comments are mine. Stookey finally concluded that his case might be a case of leishmaniasis and Dennie finally concluded that his case might be one of malignant syphilis. I have placed a somewhat different interpretation on them.

dome of the skull. Blair has reported a few such cases. It has occurred to me that these cases may be of a similar nature. Both the maxilla and the bones of the dome of the skull are membranous bones. They have little or no ability to lay down new bone and there is possibly less tendency to limitation of a low grade inflammatory process than would be the case in nonmembranous bone.

PROPHYLAXIS

A question of great importance is whether or not one should extract a tooth during the acute stage of peridental infection. Exodontists of wide experience state that in most instances early extraction of the tooth at fault will give drainage and may prevent the onset of a true osteomyelitic process. They believe that those few cases that go on to show the signs eventually of an osteomyelitic process would have done so anyway. On the other hand, surgeons who see the frank cases of osteomyelitis have been inclined to point out the dangers of extracting a tooth during the acute stage.

Probably in addition to the factors of virulency of the infection and the resistance of the patient the crux of the situation is the amount of trauma inflicted in the removal of the tooth. If the tooth can be simply and easily lifted out of its socket, it is probable that the operation is similar to the one of early trephining in an osteomyelitis of a long bone. If the infection does not have clinical signs of great virulency, early extraction with little trauma will give relief from pain and usually is generally beneficial. On the other hand, if considerable trauma is inflicted in the removal of the tooth, it would be somewhat similar to doing a radical procedure early in the course of an osteomyelitis of a long bone, a procedure long known to be distinctly contraindicated.

It probably also should be remembered that the analogy in comparison with osteomyelitis of the long bones in general breaks down somewhat so far as the organism that most often causes an osteomyelitis of the jaws is concerned. An acute peridental infection is usually caused by *Streptococcus hemolyticus*, while the organism encountered elsewhere is as a rule *Staphylococcus aureus*. This fact warns one to lean to the conservative side when in doubt.

O'Kell and Elliott ran blood cultures on a series of patients following the extraction of teeth for septic months and they found that "within a few moments after the extraction of teeth from obviously septic mouths, a transient streptococcal bacteremia lasting a few minutes may be observed in 75 per cent of cases." The observation is of great importance to the subject in hand.

From a perusal of the cases that I have seen, I would judge that one might use the same type of surgical judgment in regard to this matter that should be used in regard to an acute, subacute, or chronic osteo-

other patient (Fig. 2) had never been out of this country. In one case (Fig. 2) rabbits were inoculated with the sera of some of the involved tissue.



Fig. 3.—Second case of progressive osteomyelitis of the maxilla. The first indication of the onset of the condition followed an injury to the antrum. The osteomyelitis successively involved the frontal bones and base of skull and resulted in patient's death from a meningitis. A, Photograph taken Sept. 22, 1931; B, photograph taken Sept. 15, 1932.



Fig. 4.—A, Same patient as shown in Fig. 3. Photograph taken Sept. 15, 1932; B, photograph taken Dec. 7, 1932, at the time of his death. (Case of Stookey.)

Sometimes a pyogenic osteomyelitis develops in the frontal bone following a frontal sinusitis which progressively involves the bones of the

fore separation was complete for the purpose of relieving pain. In the 2 others nothing was done unless separation of the sequestrum was complete. In most instances the sequestrum in the syphilitic cases finally separated and was exfoliated spontaneously or was removed by forceps without anesthesia.

SUMMARY

Although frank osteomyelitis of the jaw bones is not very common, the disease, nevertheless, is of considerable seriousness and often does not receive the care most likely to effect the best results. In children, due to interference with the nonerupted teeth, the resulting deformity of growth is likely to be considerable. In both children and adults gross loss of a part of the mandible, especially, may produce a deformity and considerable disability.

Two patients who suffered from a unique chronic progressive osteomyelitis of the maxilla, base of the skull, and frontal bones which terminated in a fatal meningitis after a period of about eighteen months are described. It is suggestive that the process seemed to start in the maxillary sinus and progressively involved membranous bone.

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myelitis in bones other than the jaws. If the infection does not give the clinical signs of great virulency, if the general health of the patient is good and little trauma is necessary to extract the tooth, I should judge that early extraction may be beneficial. However, if the clinical signs of the infection suggest considerable virulency, if the patient is debilitated and it appears that the extraction would be associated with considerable trauma, early extraction should not be performed.

TREATMENT OF THE OSTEOMYELITIS

After development of a true osteomyelitis, the patients reported herein have been treated conservatively while the process was acute. As soon as definite evidence of localization of the products of inflammation occurred, the soft tissues were incised, but operation on the bone was considered contraindicated. Whenever internal incision seemed unlikely to give adequate drainage, drainage by external submandibular incision was made.

During the period between drainage of pus and sequestration, the treatment was symptomatic and supportive. When the time interval was sufficient for the sequestration to have separated, an approach was made through an incision in an inconspicuous position which allowed fairly direct approach. The sinus tract was followed; all dead bone was removed. If a sinus tract led to a tooth root or to a tooth bud, it was removed. All overhanging edges of the bone were removed. Thus, one side of the bone was sauced out so that the soft tissue could fall into the defect. For the first week the wound was gently packed open with a strip of iodoform gauze which as a rule was changed every other day.

The exception to the above procedure as to time of the sequestrectomy occurred in two patients with gross sequestration of the whole thickness of the lower jaw; in one it was deemed wise to wait six months and in a second nine months to allow sufficient new bone to form to maintain the contour of the lower face. In the majority of cases only one operation was found to be necessary to effect a cure if the operation in the chronic stage was rather thoroughly and completely performed.

NUMBER OF OPERATIONS AND PROGNOSIS

In our series the two patients with the progressive osteomyelitis of the upper jaw, base of the skull, and frontal bone, the patient with noma, the 3 patients with leucemia, and 2 of the patients with irradiation necrosis died without operation. It was judged that either the patient's general condition did not warrant any operative procedure or that the disease was of a type not amenable to surgery. Thirty-four of the pure pyogenic osteomyelitis cases were cured after one operation; 3 had more than one sequestrectomy. None of them died. In 2 cases of irradiation necrosis one-half of the mandible was resected be-

quent changes in position and postural drainage; vigorous percussion over the collapsed lobe; expectorants to thin the retained secretions (ammonium chloride or potassium iodide); and removal of the secretions by intratracheal suction or bronchoscopy.

It is a common observation that most patients cannot cough effectively after operation because of wound pain. If cough is present, it is most frequently of the weak, restrained, unproductive type, though it is obvious that tracheobronchial secretions necessitating removal are present. Morphine has been advised to relieve pain and secure more effective coughing, but this drug decreases the sensitivity of the cough reflex and depresses respiration in general; therefore, it has marked disadvantages. Capelle⁷ has shown that an increase in the vital capacity amounting to only 3 to 5 per cent follows the administration of morphine. Thus the amount of air which can be utilized in sweeping the bronchial tree free of its contained mucus is not appreciably augmented.

It may be reasoned that relief of abdominal wound pain possibly may cause restrained coughing. It is, however, unlikely that this mechanism could work in this direction, since cough results from stimulation of the respiratory mucosa by the presence of foreign material in the air passages. Thus, pain in the wound could logically serve only to inhibit the action of the muscles of respiration or more specifically the abdominal muscles which are so necessary for forcible and effective coughing.

Because of these facts I have reasoned that elimination of wound pain by means of paravertebral novocain block would produce an increased pulmonary ventilation and more effective cough reflex. If this method could be used both prophylactically and therapeutically in atelectasis it seemed that this would be a particularly promising procedure with which to combat postoperative atelectasis.

Several preliminary observations were carried out at Presbyterian Hospital, New York City, in an attempt to measure the relative changes in thoracic and abdominal excursion in postoperative cases after paravertebral block. These experiments showed some augmentation in the diaphragmatic component. In an attempt to secure prolonged anesthesia a local anesthesia in oil (neothesol) commonly used in anorectal surgery was tried in a few cases without conclusive results. This work is to be continued.

In the meantime, however, two cases* of atelectasis following appendectomy were encountered in children. Such remarkable results followed the induction of paravertebral block anesthesia of the wound that I believe this method to be of sufficient value to report at this time.

CASE 1.—R. A., male, aged 7 years. The patient was admitted to Doernbecher Hospital for Children on Jan. 19, 1940, with a history of diarrhea of three days'

*Since this paper was submitted a third case presenting essentially the same picture was treated in a similar manner with equally satisfactory results.

PARAVERTEBRAL PROCAINE BLOCK IN THE TREATMENT OF POSTOPERATIVE ATELECTASIS

A PRELIMINARY REPORT

JOHN A. GIUS, M.D., MED. SC.D., PORTLAND, ORE.

(From the Department of Surgery, University of Oregon Medical School)

WITHIN recent years the importance of atelectasis as the predominant early postoperative pulmonary complication and the primary condition in the development of postoperative pneumonia has been widely recognized. In a review of the literature published elsewhere¹ the different aspects of the problem, including pathogenesis and treatment, have been discussed.

Many authors (Head,² Powers,³ Patey,⁴ Carlson,⁵ Beecher,⁶ Capelle⁷) agree that pulmonary hypoventilation occurs after nearly all abdominal operations. This appears to be the result of the incision placed in the abdominal wall which directly and reflexly interferes with abdominal and diaphragmatic excursion. That this effect is particularly marked after upper abdominal operations is in agreement with the clinical observation that incidence of pulmonary complications is greatest after operations on the stomach and duodenum, biliary tract, pancreas, and spleen. Most of this impairment of ventilation can be ascribed to wound pain producing voluntary inhibition and reflex spasm of the abdominal muscles as well as the diaphragm itself.⁷ That the diaphragm following operation is high and relatively immobile has been repeatedly observed. The frequency with which transient physical signs can be demonstrated in the right lower lobe is another manifestation of this impairment of function. Capelle⁷ has shown that continuous anesthesia of the abdominal wound will result in reactivation of the diaphragm as well as a return of the vital capacity from the usual 20 to 40 per cent immediately after operation to 90 per cent of normal.

In addition to hypoventilation another significant predisposing factor exists, the loss of the ability to cough effectively following operation. Secretions which are normally removed by cough, ciliary action of the bronchial epithelium, and peristaltic activity of the bronchioles tend to thicken and adhere to the bronchial walls and thus may be removed incompletely or only with great difficulty. If the patient is unable or unwilling to cough, the mucus may remain and produce lobular or even lobar obstruction. Absorption of the air entrapped distally soon occurs and atelectasis results. Unless vigorous measures are promptly undertaken to remove the obstructing mucus, organisms usually derived from the upper respiratory passages invade the collapsed area and produce the much more serious complication, pneumonia.

The most effective measures for securing evacuation of the plug and re-expansion of the collapsed area are: active hyperventilation and cough, either voluntarily or by means of carbon dioxide inhalations; fre-

Paravertebral block was done (Dr. V. Larson) with 1 per cent procaine with cobefrin solution. Four cubic centimeters were deposited in each of the following spaces: dorsal 10, 11, 12, and lumbar 1 and 2. Immediately following the block the patient began to cough effectively and without pain in the wound. He was

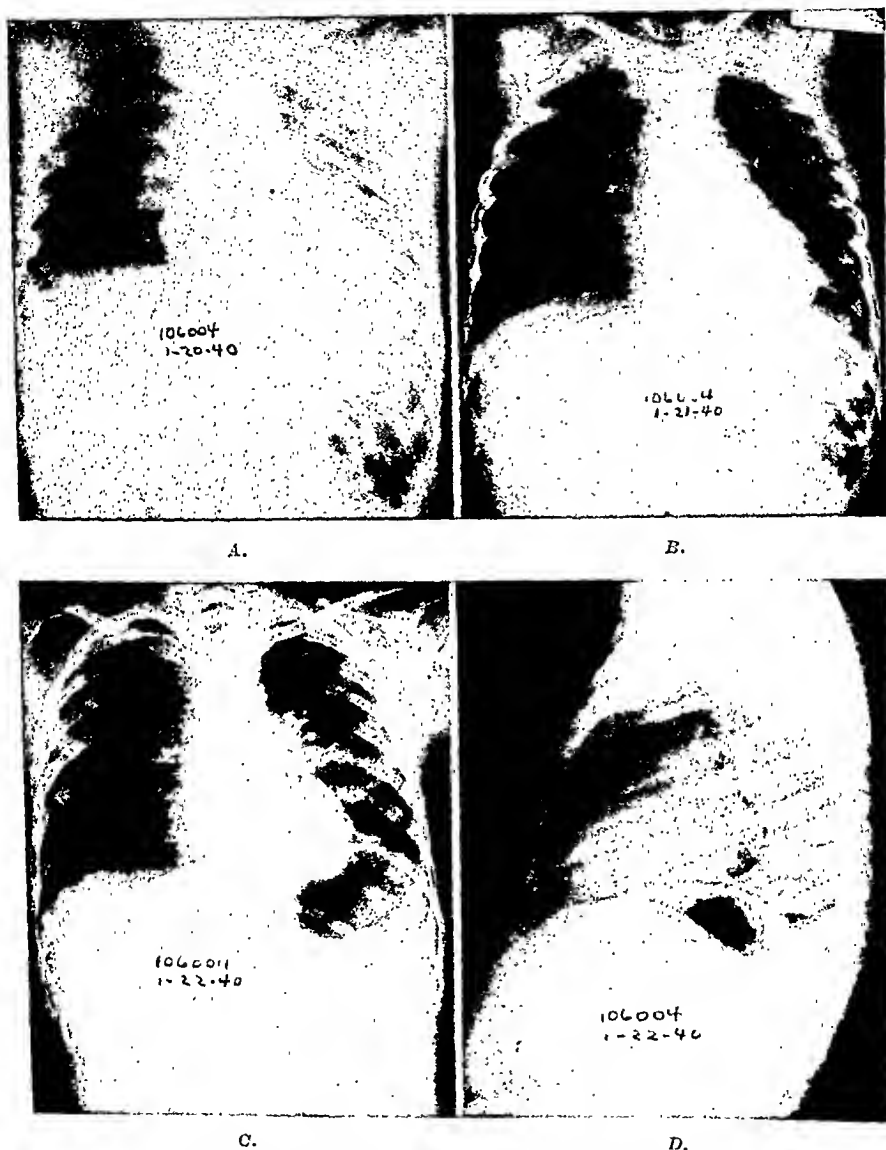


Fig. 2.—Case 1. A, (Jan. 20, 1940) There is a suggestion of an increased density at the left base behind the heart. There is definite narrowing of the fourth to eighth rib interspaces. B, (Jan. 21, 1940) The film shows a definite density behind the heart on the left, as well as narrowed rib interspaces. C, D, (Jan. 22, 1940) There is definite diminution in the density at the right base. The diaphragm is elevated because of gas in the stomach. A film taken on Jan. 21, 1940, showed the lung fields to be clear.

placed in the lateral position with the foot of the bed elevated, turned frequently, given carbon dioxide inhalation every hour, and ammonium chloride 10 grains every four hours.

He continued to cough voluntarily during the remainder of the day, and small amounts of mucus were expectorated. By evening the temperature had fallen to

duration. On Jan. 18 he developed lower abdominal pain and vomiting. Castor oil had been administered on the day of onset of symptoms. During the preceding week the patient had been convalescing from the "flu" and during this time had had some nasal discharge, cough, malaise, and anorexia.

The essential physical findings consisted of a temperature of 100.8° F.; pulse, 88; respiration, 22. The nose and pharynx were definitely injected. The tonsils were large and infected. Heart and lungs were negative. Moderate tenderness and spasm were found in the right lower quadrant. Urinalysis was negative except for acetone + + +, diacetic +. White blood count, 25,000; polymorphonuclear leucocytes, 79; small lymphocytes, 13; monocytes, 4; sedimentation rate, 9 first 15 minutes, 43 in 45 minutes. *Clinical Diagnosis:* Acute appendicitis, subsiding influenza.

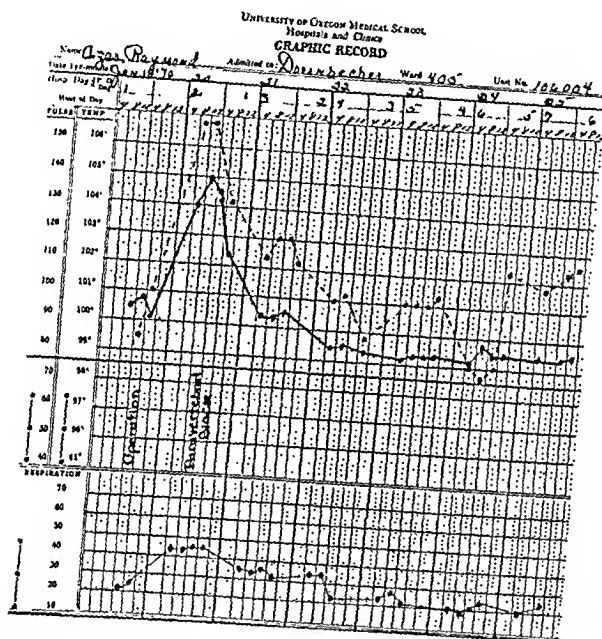


Fig. 1.

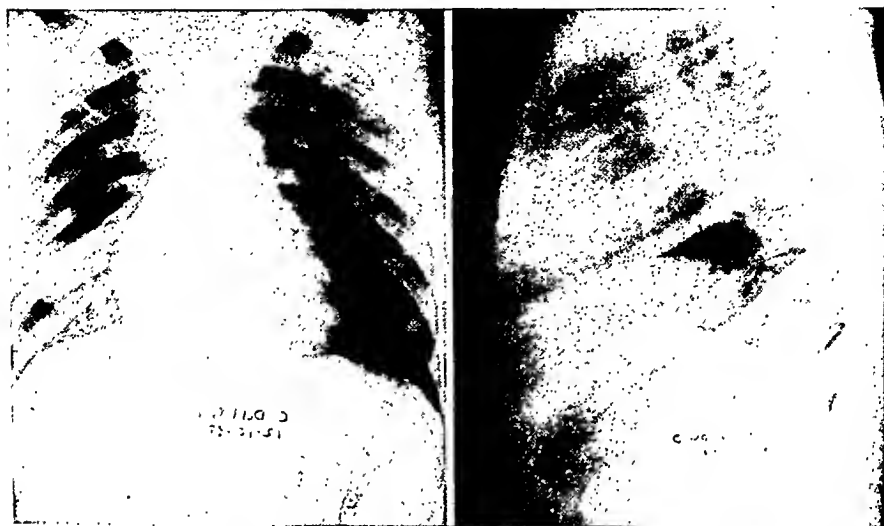
An infusion of 750 c.c. 5 per cent glucose in saline was given and appendectomy was performed through a McBurney muscle-splitting incision under open-drop ether anesthesia. A large, acutely inflamed appendix with a small abscess was found. Cultures of the abscess later showed gram-negative rods, resembling *B. influenzae* and a few hemolytic streptococci. A Penrose drain was placed down to the peritoneum and the wound was closed loosely.

Postoperatively the patient was given parenteral fluids and codeine. On the first day after operation the temperature spiked to 105° F. and the pulse and respiration rose to 160 and 44 respectively (Fig. 1). It was noted that the patient was trying to inhibit cough which seemed dry and unproductive. Attempts to get him to cough were of no avail on account of pain in the wound.

Examination of the chest revealed a slight lag on the left. Some suppression of breath tones and dullness were noted over both lower lobes posteriorly near the spine. The breath tones had a bronchial quality in the region of the left hilum. There was no demonstrable mediastinal shift.

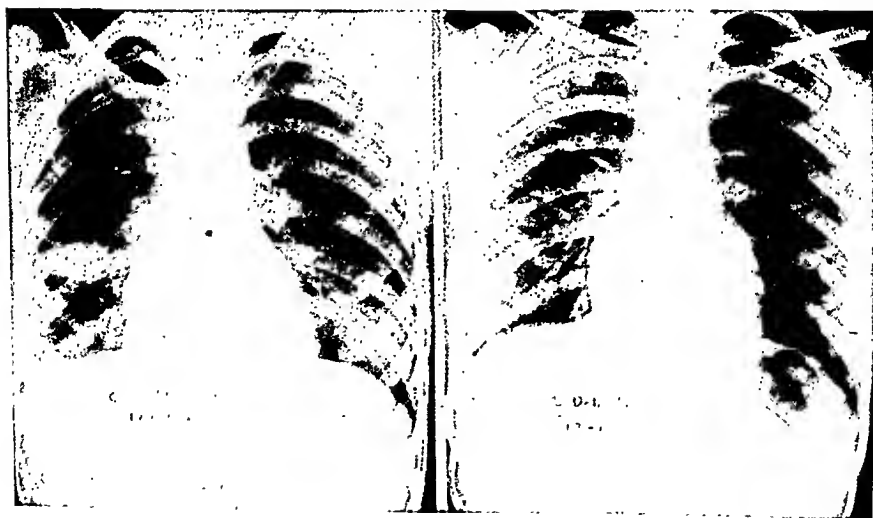
X-ray of chest showed some increased density of the left base with narrowing of the intercostal spaces, no mediastinal shift. Impression: Atelectasis left lower lobe.

temperature to 101° F. (Fig. 3), but no abnormal symptoms or signs were noted. On the second day the temperature was 103° F.; pulse, 110; and respirations, 26, at 8:00 A.M. At this time a moist productive cough was observed and the patient complained of a great deal of wound pain when coughing. Examination of the chest



A.

B.



C.

D.

Fig. 4.—Case 2. A, B, (Dec. 10, 1939) Posteroanterior and lateral x-rays. There is a triangular shaped area of increased density in the upper portion of the right lower lobe posteriorly. There is no apparent change in the level of the right leaf of the diaphragm, width of the rib interspaces, or the position of the mediastinum. C, (Dec. 11, 1939) There is a suggestion of a decrease in the density in the right lower lobe. D, (Dec. 14, 1939) The lung fields are clear.

showed decreased expansion on the right, dullness to flatness over the right lower lobe both posteriorly and in the axilla, and distant breath sounds over this area.

An x-ray (Fig. 4A) confirmed the diagnosis of right lower lobe atelectasis and a paravertebral procaine block was performed by Dr. John Hutton. Five cubic centimeters of a 1 per cent novocain solution with cobefrin was injected into each of

102.2° F., and it was found that the lung fields had cleared somewhat. However, there was still some suppression of the breath tones and impaired resonance at the left base. No râles were heard.

On the following day the temperature was 100.4° F.; pulse, 120; respirations, 32. Cough was vigorous but not very productive. The chest signs were somewhat less marked than previously, but some suppression of breath tones persisted. These cleared on the following day and except for slight drainage from the wound the remainder of the convalescence was uneventful.

CASE 11.—(No. 37012.) C. D., female, aged 11 years, was admitted to Doernbecher Hospital for Children on Dec. 8, 1939, for pain in the lower abdomen of one day's duration. The patient had had a cold for a week which was apparently clearing satisfactorily. On the night before admission she had complained of epigastric pains which were later referred to the right lower quadrant. There had been no nausea or vomiting. Some constipation had been noted previously, but no cathartics had been administered. The past history was negative.

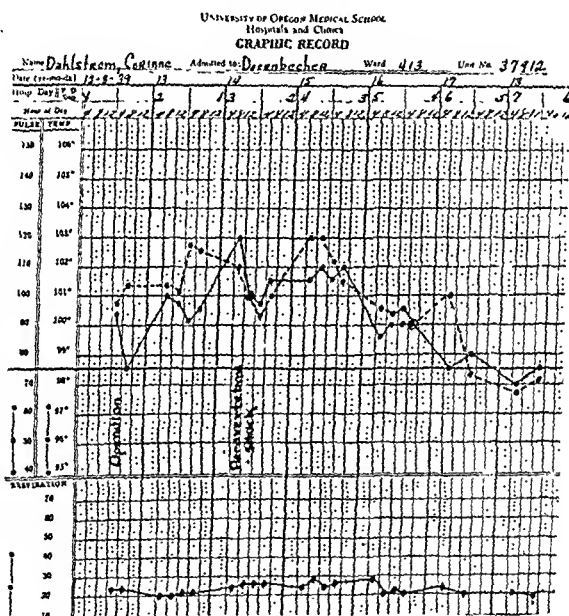


Fig. 3.

Physical Examination: Temperature, 100.4° F.; pulse, 82; respirations, 19. The nose and throat were definitely injected. The chest was resonant and clear throughout. The abdomen was flat and there were marked tenderness and muscle spasm over McBurney's point. Some tenderness was noted high on the right on rectal examination. Urinalysis was negative. White blood count, 12,700; polymorphonuclear leucocytes, 79; small lymphocytes, 16; polymorphonuclear eosinophiles, 1; monocytes, 1; staff cells, 3; sedimentation rate, 15 minutes, 4 mm., and 45 minutes, 28 mm.

Clinical Diagnosis: Acute appendicitis; resolving common cold.

Anesthesia: Cyclopropane, premedication, atropine sulfate gr. $\frac{1}{200}$, sodium phenobarbital gr. $\frac{3}{4}$.

Operation: Appendectomy, McBurney muscle-splitting incision, no drains.

Pathologic Diagnosis: Acute suppurative appendicitis.

Postoperative Course: On the first postoperative day the pulse rose to 118 and

A STUDY OF CAPILLARY PERMEABILITY AND INFLAMMATION IN THE SKIN OF RABBIT GIVEN ADRENALIN*

R. H. RIGDON, M.D., MEMPHIS, TENN.

(From the Department of Pathology, University of Tennessee Pathological Institute†)

PREVIOUS experiments have shown that trypan blue given intravenously will localize and concentrate in areas of skin treated with xylol only when this irritant is applied within a period of less than three hours preceding the injection of the dye. Xylol applied to the normal skin of the rabbit produces hyperemia within twenty to sixty seconds. This hyperemia is subsequently followed by edema and an infiltration of the area with leucocytes.¹ Hyperemia apparently results from a dilatation of the capillaries, venules, and arterioles. Lewis² has suggested that such a reaction may result from a local chemical change connected with tissue metabolism and that it is independent of nerve control, either central or local.

Adrenalin injected intradermally produces blanching of the rabbit's skin. Lewis² states that this drug acts directly upon the arterioles, capillaries, and venules. Cotton and his associates³ concur with Lewis. Krogh⁴ has expressed the opinion that the effects of adrenalin on the capillaries are produced through its action on the Rouget cells. All physiologists, however, are not in agreement with Krogh. Some hold that the contraction of the capillaries results from the direct action of the drug on the endothelial cells.

Pickrell⁵ recently has shown that rabbits narcotized with alcohol or ether show only a few polymorphonuclear leucocytes in areas of skin where pneumococci and aureonate were injected. Cressman and I,⁶ also studying the effects of anesthesia on capillary permeability and inflammation, injected staphylococci, pneumococci, and aureonate intradermally in rabbits anesthetized with alcohol, ether, and nembutal. Some of our animals narcotized with alcohol or ether did not develop a local inflammatory reaction, while other rabbits given the same anesthesia did show a reaction similar to that in the controls. All the rabbits narcotized with nembutal and injected with the same bacteria, however, developed an inflammatory reaction similar to that in the controls.

It is well known that adrenalin will counteract the swelling induced by the application of irritants to the skin. The edema produced by histamine may also be prevented by the injection of adrenalin. In view of this action of adrenalin on the vascular system it was thought important to study its effect on capillary permeability and the development of an inflammatory reaction at the site of injection of a saline suspension of staphylococci.

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the following interspaces: dorsal 10, 11, 12, and lumbar 1. Relief of all pain was noted on completion of the block.

Immediately following this procedure the patient began to cough vigorously and expectorated large quantities of mucopurulent sputum. An abdominal binder was applied and the patient was encouraged to cough and was aided in evacuating the secretions by frequent changes in position, percussion over the chest, carbon dioxide inhalations, and ammonium chloride 10 grains every four hours. Three hours later examination revealed some persistent dullness, but the breath tones came through much clearer than previously. During the third and fourth postoperative days the patient continued to cough up moderate amounts of sputum and the chest signs rapidly cleared. On the fifth postoperative day there was no further cough or abnormal signs in the chest.

The possibility of separation of the operative wound following violent coughing must be borne in mind and support of the abdominal wall is indicated. During the period when atelectasis is most likely to occur, the catgut sutures are said to retain their maximum strength. It is true that the added strain of severe coughing occasionally may break or tear out the sutures, but urgent measures are warranted if the more serious pulmonary complications are to be avoided.

I am perfectly aware that the prognosis in postoperative atelectasis is good and resolution occurs in the majority of cases following the usual methods of treatment. The results in these two cases, however, were so striking that there seems to be no doubt that the production of anesthesia in the wound played a significant role in the rapid clearance of symptoms and signs. These cases can hardly be regarded as a conclusive test of a procedure, yet the results observed in the three cases where prophylactic injection was carried out and the two cases reported here convince me that this method of treatment is of practical value.

CONCLUSION

Two cases of postoperative atelectasis which were successfully treated by paravertebral block anesthesia of the operative wound are reported. It is suggested that this procedure which temporarily abolishes pain in the wound and allows for active hyperventilation of the lungs and effective coughing may prove to be an important adjunct to the usual methods now utilized in combating this condition.

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The skin, however, becomes reddish brown in color where xylol is applied in the rabbits treated with xylol either before or after the intradermal injection of the adrenalin. This peculiar color appears fifteen to thirty minutes following the application of the xylol. The larger blood vessels in these areas of skin appear dilated. Fig. 1 shows the reddish brown color of the skin in a rabbit given adrenalin intradermally after which xylol was applied to the local areas. Two-tenths cubic centimeter of adrenalin was injected intradermally into the center of Areas 1 and 2. Xylol was then applied to the skin in Area 1 five minutes later. Xylol was also applied at this time to Area 3. The skin was blanched in Areas 1 and 2 at the time the xylol was applied to the

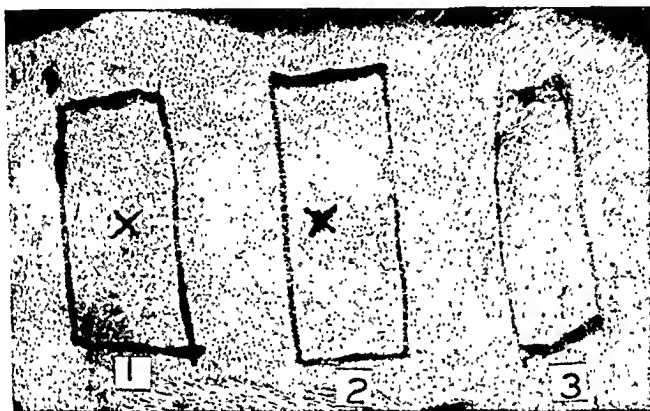


Fig. 1.—Hyperemia in areas of skin treated by the local application of xylol. Two-tenths cubic centimeter adrenalin, 1:1,000 dilution, was injected intradermally at X in Areas 1 and 2. Xylol was applied over Areas 1 and 3 five minutes later. The skin in Area 3 was hyperemic after one minute. Area 3 was hyperemic after fifteen minutes. Area 2 was pale in color at this time. Area 1 was reddish brown in color after two and one-half hours and Areas 2 and 3 were blanched at this time.

skin in Area 3. The skin was also hyperemic in Area 3 five minutes following the application of xylol. This hyperemia decreased, however, after ten to twenty minutes. This diminution in hyperemia apparently followed a diffusion of the adrenalin from Area 2 into Area 3. Such a decrease in the hyperemia as observed here never occurs when the adrenalin is injected in the skin on one side of the rabbit and the xylol is applied to the skin on the opposite side. The skin in Area 1 was slightly reddish brown in color fifteen minutes following the application of the xylol. This color gradually increased in intensity for approximately two hours. Fig. 1 was made two and one-half hours following the application of the xylol.

The following experiment illustrates the changes in color which occur in the skin following the intradermal injection of both adrenalin and saline solution and also the localization and concentration of trypan blue in xylol treated areas of skin in the presence of both saline and adrenalin. Four areas were outlined on the skin on the right (Fig. 2, 1, 2, 3, and 4) and three on the left (Fig. 2, 5, 6, and 7); 0.3 c.c. of saline

METHODS AND MATERIAL

Rabbits were used in this study. They were carefully shaved twenty-four hours or more before the experiment was begun. Several areas of skin, approximately 2 by 2 cm., were outlined with India ink in those experiments where xylol was used as the local irritant. Duplicate observations were usually made in each animal.

Xylol on a cotton swab was lightly applied to local areas of skin. Care was taken not to traumatize the tissue. A 10 c.c. volume of 0.2 per cent solution of trypan blue was given intravenously immediately following the application of xylol. A record was made of the time when xylol was applied in those experiments where an interval elapsed before the dye was given. The intensity of the local staining of the skin was influenced by the interval between the application of the irritant and the intravenous injection of the dye.

The adrenalin was diluted 1:1000 (Parke-Davis preparation). It was given intravenously in the marginal ear vein in those experiments in which the systemic effects were studied. It was injected intradermally into the blebs produced by the staphylococci when the local effects were studied and also intradermally into the xylol-treated areas of skin when its local effects on capillary permeability were observed. The amount of adrenalin and the frequency with which it was injected varied with different rabbits; usually 0.2 to 0.5 c.c. was given either intradermally or intravenously at each injection. The frequency of the intravenous injections and the amount of adrenalin were influenced by the general appearance of the animal. The quantity of adrenalin given to the different animals is illustrated by subsequent data.

Five-tenths cubic centimeter of an eighteen- to twenty-four-hour broth culture of a nontoxic producing strain of staphylococci was injected intradermally to produce the local areas of inflammation. A quantity of physiologic saline solution equal to the adrenalin was injected into corresponding areas for the control observations on the same animal. The skin at the site of injection of the bacteria was removed after six to eight hours and fixed in a 10 per cent solution of formalin. Sections were stained routinely with hematoxylin and eosin. Select sections were stained by Giemsa's method to demonstrate the bacteria.

CAPILLARY PERMEABILITY IN LOCAL AREAS OF THE RABBIT'S SKIN IN THE PRESENCE OF ADRENALIN INJECTED INTRADERMALLY

The first experiment is a study of the influence of local injections of adrenalin on the localization and concentration of trypan blue in areas of rabbit's skin treated with xylol.

The vascular constriction which normally follows the intradermal injection of adrenalin extends outward for several centimeters from the point of inoculation. This blanched reaction remains for several hours.

The skin, however, becomes reddish brown in color where xylol is applied in the rabbits treated with xylol either before or after the intradermal injection of the adrenalin. This peculiar color appears fifteen to thirty minutes following the application of the xylol. The larger blood vessels in these areas of skin appear dilated. Fig. 1 shows the reddish brown color of the skin in a rabbit given adrenalin intradermally after which xylol was applied to the local areas. Two-tenths cubic centimeter of adrenalin was injected intradermally into the center of Areas 1 and 2. Xylol was then applied to the skin in Area 1 five minutes later. Xylol was also applied at this time to Area 3. The skin was blanched in Areas 1 and 2 at the time the xylol was applied to the

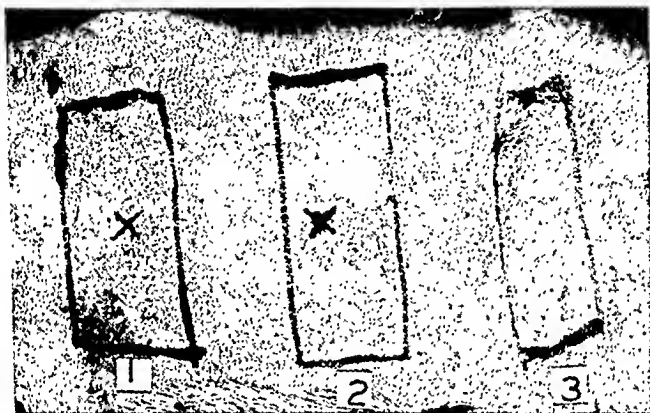


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solution was injected intradermally in each of the areas on the right and 0.3 c.c. of adrenalin was injected intradermally into each of the areas on the left. Xylol was applied over Areas 1 and 5 immediately following the injection of the saline solution and the adrenalin. Six hours later xylol was applied to the skin in Areas 2, 4, and 7. Ten cubic centimeters of a 0.2 per cent solution of trypan blue was given intravenously immediately following the last application of xylol. The skin was



Fig. 2.—Rabbit 481; localization and concentration of trypan blue in areas of rabbit's skin treated with xylol. These areas were previously injected intradermally with 0.3 c.c. saline solution and adrenalin. Areas 1, 2, 3, and 4 were injected with saline solution and Areas 5, 6, and 7 with adrenalin. Xylol was applied over Areas 1 and 5 immediately following the injection of the saline solution and the adrenalin. Xylol was applied over Areas 2, 4, and 7 six hours later. Trypan blue was injected intravenously immediately following the last application of xylol. The dye localized only in Areas 2 and 4. Photographed after thirty minutes.

blanched in Areas 5, 6, and 7 fifteen minutes following the injection of the dye. The skin in Areas 2 and 4 was blue at this time. There was no dye in either Area 1, where saline solution was injected and xylol was applied six hours previously, or in Area 7, where adrenalin was injected and xylol was applied. Trypan blue was present only in Areas 2 and 4 (Fig. 2).

A STUDY OF CAPILLARY PERMEABILITY IN THE SKIN FOLLOWING
INTRAVENOUS INJECTIONS OF ADRENALIN

Seven rabbits were used in this second experiment. Xylol was applied to local areas of the skin both before and after the intravenous injection of the adrenalin. The normal skin and the hyperemia produced by xylol blanched following the first intravenous injection of adrenalin. The skin then remained pale throughout the experiment. A protocol on one rabbit illustrates the changes observed in the skin and also the effects produced by adrenalin on the localization and concentration of trypan blue following the local application of xylol.

| | | |
|------------|--|----------------------|
| 11:15 A.M. | 0.2 c.c. adrenalin intravenously | xylol applied Area 1 |
| 11:26 | 0.2 c.c. adrenalin intravenously | xylol applied Area 2 |
| 11:35 | 0.2 c.c. adrenalin intravenously | xylol applied Area 3 |
| 11:40 | | xylol applied Area 4 |
| 11:45 | 0.2 c.c. adrenalin intravenously | xylol applied Area 5 |
| 11:46 | 15 c.c. of 0.2 per cent trypan blue intravenously | |
| 11:50 | Area 5; the skin is light blue | |
| 11:51 | Area 4; the skin is light blue | |
| 11:55 | Trypan blue is present in Areas 3, 4, and 5 | |
| 1:00 P.M. | Trypan blue is present in Areas 1, 2, 3, 4, and 5; there is a progressive decrease in the intensity of color, however, in Area 5 to Area 1 | |

The dye did not appear in the xylol-treated areas of skin as quickly in some of the rabbits given a larger quantity of adrenalin as it did in the rabbit shown in the above protocol. Such variations, however, are observed in normal rabbits.

All of these experiments show that trypan blue localizes and concentrates in the xylol-treated areas of skin even when there is a quantity of adrenalin in the circulating blood sufficient to produce vascular constriction and inhibits the hyperemia that normally occurs following the local application of xylol.

EFFECTS OF ADRENALIN GIVEN INTRADERMALLY ON THE INFLAMMATORY
REACTION PRODUCED BY STAPHYLOCOCCI

The results obtained in the preceding experiments show that adrenalin injected intradermally inhibits the localization and concentration of trypan blue in areas of skin treated with xylol, while adrenalin injected intravenously does not prevent the localization and concentration of trypan blue in areas of skin treated with xylol, although it may inhibit the development of hyperemia and edema.

Seven rabbits were used in the third experiment to study the effect of adrenalin injected intradermally on the local inflammatory reaction produced by staphylococci. Four areas were injected intradermally with the broth culture of staphylococci. Adrenalin was injected immediately in two of these four areas and a similar quantity of saline solution was injected at the same time into the other two areas. The injection of

the adrenalin and the saline solution was repeated after two to four hours.

The skin in the areas injected with staphylococci and saline solution was hyperemic and edematous, while the areas injected with staphylococci and adrenalin usually showed neither hyperemia nor edema after six hours. Histologic studies of the skin in five of the seven rabbits showed a marked diminution in the number of polymorphonuclear leucocytes in the tissues about the staphylococci in the areas injected with adrenalin as compared with the corresponding areas in the same animal injected with saline solution (Fig. 3). Only one rabbit in the group



Fig. 3.—Rabbit 510; 0.3 c.c. of an infusion broth culture of staphylococci was given intradermally into four areas. Three-tenths cubic centimeter adrenalin was injected intradermally into two of these blebs immediately thereafter and 0.3 c.c. saline solution was injected at the same time into the other two blebs. The injections of the saline solution and the adrenalin were repeated after two blebs. The injections of the killed eight hours after the staphylococci were injected. Area 1 was injected with saline solution. Area 2 was injected with adrenalin. Note the difference in the number of the leucocytes in the tissue. There are masses of bacteria in Area 2.

showed approximately the same number of leucocytes about the staphylococci in the areas injected with adrenalin as were present in the areas injected with saline solution.

The degree of phagocytosis by individual leucocytes is the same in all sections regardless of the presence of either saline solution or adrenalin.

EFFECT OF INTRAVENOUS INJECTIONS OF ADRENALIN ON THE INFLAMMATORY REACTION PRODUCED BY STAPHYLOCOCCI

In the preceding experiment it was found that the number of leucocytes were decreased in areas of skin where adrenalin was injected intra-

dermally as compared with similar areas of skin injected intradermally with saline solution. Six rabbits were used in this experiment to determine the effect of adrenalin, when given intravenously, on the inflammatory reaction produced by staphylococci. Four rabbits were used in the control group. The frequency of the injections and the amount of adrenalin are illustrated by the following experiment:

| | |
|------------|--|
| 9:35 A.M. | 0.25 c.c. adrenalin intravenously |
| 9:50 | 0.2 c.c. adrenalin intravenously |
| | 0.2 c.c. of eighteen-hour infusion broth culture of staphylococci injected intradermally into four areas |
| 10:00 | 0.2 c.c. adrenalin intravenously |
| 10:20 | 0.2 c.c. adrenalin intravenously |
| 11:00 | 0.2 c.c. adrenalin intravenously |
| 11:30 | 0.2 c.c. adrenalin intravenously |
| 12:00 | 0.2 c.c. adrenalin intravenously |
| 12:45 P.M. | 0.2 c.c. adrenalin intravenously |
| 1:30 | 0.2 c.c. adrenalin intravenously |
| 2:10 | 0.2 c.c. adrenalin intravenously |
| 3:10 | 0.2 c.c. adrenalin intravenously |
| 3:50 | Killed, section of the skin injected with staphylococci removed for histologic studies |

One of the rabbits in this group died four hours after the experiment was begun. The four areas injected with staphylococci in this animal did not show any hyperemia, edema, or leucocytes. Two of the remaining five rabbits also did not show either hyperemia or edema in the areas of skin injected with the staphylococci. There was some diminution in the number of leucocytes about the organisms in these two animals as compared with the controls. Three of the five rabbits, however, showed both hyperemia, edema, and essentially the same number of leucocytes about the staphylococci as were present about the bacteria in the control animals.

DISCUSSION

These experiments show that trypan blue when given intravenously does not localize in xylol-treated areas of skin when adrenalin is injected intradermally into the same area. These observations suggest that adrenalin either prevents an increase in capillary permeability or this drug produces complete vascular occlusion and thereby prevents any of the dye from reaching the local areas of the skin. The presence of a reddish brown color in the skin thirty minutes following the intradermal injection of adrenalin and the local application of xylol indicates that certain vascular channels must be patent. It is interesting to recall in regard to this reaction that Krogh⁴ found the vessels in inflamed tissue unresponsive to adrenalin. The failure of the xylol-treated areas of skin to stain blue following the intravenous injection of trypan blue may be explained, therefore, on a failure of the individual cells to stain rather than upon the failure of the dye to reach the area.

These observations furthermore suggest that the local staining of xylol-treated areas of rabbit's skin by trypan blue may represent not only an increase in the permeability of the capillaries, but also a change occurring in the permeability of the tissue cells. Kline and Winternitz⁷ state that the nucleus of a living cell never stains vitally, but as soon as a cell is injured its nucleus absorbs the stain. In view of the observation of Kline and Winternitz it would appear likely that the staining of an area of skin treated with xylol may indicate that some change occurs in the tissue cells following the application of this irritant rather than that the localization of trypan blue indicates only an increase in capillary permeability. Adrenalin apparently may inhibit either the adsorption or the absorption of trypan blue by the cell, although the latter may be injured.

It is interesting to note that in these experiments the hyperemia may be absent in the skin of rabbits in which adrenalin is given intravenously; however, when trypan blue is given intravenously, it localizes and concentrates in these areas of skin recently treated with xylol. This experiment indicates that hyperemia is not essential for the localization and concentration of trypan blue. Previous experiments have also shown that hyperemia and edema are not essential for the localization and concentration of trypan blue.¹ Increase in capillary permeability as shown by the localization of trypan blue may frequently occur, however, in tissues when they are hyperemic and edematous.

The failure of leucocytes to localize in the tissue about staphylococci, when adrenalin is injected intradermally, may be explained by vascular obstruction and a failure of the leucocytes to reach the area. The presence of leucocytes, however, about the staphylococci in the rabbits given adrenalin intravenously may be due to the low concentration of this drug in the local tissue. There was a complete absence of leucocytes about the staphylococci in two rabbits given adrenalin intravenously. It does not appear likely that the absence of leucocytes can be accounted for through the direct effect of adrenalin on the local blood vessels. The amount of adrenalin given to five rabbits in this experiment was sufficient to prevent the occurrence of either hyperemia or edema, but apparently it was an insufficient quantity to prevent the localization of polymorphonuclear leucocytes about the bacteria.

The results obtained in this study would suggest that xylol when applied locally injures tissue cells and such cells may then either adsorb or absorb trypan blue dyes. The period in which the epithelial cells remain permeable to trypan blue is approximately three hours following the application of xylol. The localization and concentration of trypan blue in areas of injury may be an index of increased capillary permeability, but it apparently is also an indication of the duration in which a cell is injured.

SUMMARY

Adrenalin given intradermally or intravenously in large quantities inhibits the development of hyperemia in the skin where xylol is applied. Trypan blue, when given intravenously, fails to localize and to concentrate in areas of rabbit's skin where adrenalin is injected intradermally and xylol is applied locally although the area becomes reddish brown in color after twenty to thirty minutes. Trypan blue localizes and concentrates in areas of the skin treated with xylol when the rabbit is given large quantities of adrenalin intravenously. This variation in the localization of trypan blue in areas of inflammation in rabbits given adrenalin intravenously and intradermally may be explained by a difference in the concentration of the drug in the local areas of tissue.

The number of polymorphonuclear leucocytes is decreased around staphylococci when adrenalin is injected intradermally. There is usually also a diminution in the cellular reaction around groups of staphylococci in those animals given large quantities of adrenalin intravenously. The failure of leucocytes to reach an area of skin infiltrated with staphylococci when the animal is given large quantities of adrenalin intradermally or intravenously apparently may be the result of vascular constriction. The number of leucocytes within the blood vessels in such areas of inflammation is less than in the controls.

The failure of trypan blue to localize in areas of skin where xylol is applied and adrenalin is injected intradermally would suggest that hyperemia and an increase in capillary permeability as manifested by a localization and a concentration of trypan blue do not necessarily have to occur simultaneously. Furthermore, the staining of an area of inflammation in the skin of a rabbit suggests that the permeability of the tissue cells as well as the endothelial cells of the capillaries is changed following the local application of xylol.

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These observations furthermore suggest that the local staining of xylol-treated areas of rabbit's skin by trypan blue may represent not only an increase in the permeability of the capillaries, but also a change occurring in the permeability of the tissue cells. Kline and Winternitz⁷ state that the nucleus of a living cell never stains vitally, but as soon as a cell is injured its nucleus absorbs the stain. In view of the observation of Kline and Winternitz it would appear likely that the staining of an area of skin treated with xylol may indicate that some change occurs in the tissue cells following the application of this irritant rather than that the localization of trypan blue indicates only an increase in capillary permeability. Adrenalin apparently may inhibit either the adsorption or the absorption of trypan blue by the cell, although the latter may be injured.

It is interesting to note that in these experiments the hyperemia may be absent in the skin of rabbits in which adrenalin is given intravenously; however, when trypan blue is given intravenously, it localizes and concentrates in these areas of skin recently treated with xylol. This experiment indicates that hyperemia is not essential for the localization and concentration of trypan blue. Previous experiments have also shown that hyperemia and edema are not essential for the localization and concentration of trypan blue.¹ Increase in capillary permeability as shown by the localization of trypan blue may frequently occur, however, in tissues when they are hyperemic and edematous.

The failure of leucocytes to localize in the tissue about staphylococci, when adrenalin is injected intradermally, may be explained by vascular obstruction and a failure of the leucocytes to reach the area. The presence of leucocytes, however, about the staphylococci in the rabbits given adrenalin intravenously may be due to the low concentration of this drug in the local tissue. There was a complete absence of leucocytes about the staphylococci in two rabbits given adrenalin intravenously. It does not appear likely that the absence of leucocytes can be accounted for through the direct effect of adrenalin on the local blood vessels. The amount of adrenalin given to five rabbits in this experiment was sufficient to prevent the occurrence of either hyperemia or edema, but apparently it was an insufficient quantity to prevent the localization of polymorphonuclear leucocytes about the bacteria.

The results obtained in this study would suggest that xylol when applied locally injures tissue cells and such cells may then either adsorb or absorb trypan blue dyes. The period in which the epithelial cells remain permeable to trypan blue is approximately three hours following the application of xylol. The localization and concentration of trypan blue in areas of injury may be an index of increased capillary permeability, but it apparently is also an indication of the duration in which a cell is injured.

unwilling to assume that responsibility. During the course of the next ten years, repeated efforts were made to get some recognized authority to establish a control over sterile surgical products. The Hospital Standardization Committee of the American College of Surgeons was appealed to, but claimed that they had no funds or laboratory space which could be used for the purpose. The American Medical Association was therefore called upon for help and appointed a Committee from members of the Surgical Section of the Association to study the problem. This Committee believed that it would be wise to set up not only a standard of sterility for catgut but standards of other desirable physical properties, such as size, tensile strength, and absorbability. The Committee studied the problem carefully, recommended a complete set of catgut standards, and advised the American Medical Association to set up a continuous control. This proposal was turned down by the A. M. A. The reason given was that it was thought that the situation had improved to such an extent that there was no longer any need for such a control and therefore the expense would be unwarranted. The matter was referred to the Council on Pharmacy and Chemistry. This body assigned one of its members to investigate the situation and after a year's study it was found that conditions had considerably improved in the course of ten years, but that unsterile catgut was still being sold.

The New York Academy of Medicine's Committee on Public Health Relations then became interested and promised to establish some kind of control if it were not possible to persuade some governmental agency to do so. About this time the Food and Drugs Administration was asked to examine a lot of suspected catgut and found it to be unsterile. They at once confiscated the goods and began a court action against the offending firm, on the assumption that the Pure Food and Drugs Act had been violated. Their contention was upheld by the court, but the case was appealed on the basis of the assertion that catgut was not a drug and therefore the sale of unsterile catgut was not a violation of the Act.

This uncertainty was clarified when the new Food and Drugs Act was formulated and adopted last year. It is specifically stated therein that not only catgut but also all sterile surgical supplies, including cotton, gauze compresses, bandages, band-aids, first aid dressings, adhesive plaster, plaster of Paris, etc., are drugs because they are used in the treatment of disease. If they are put out as sterile goods to be introduced into the human body or applied to its surface, there must be no contamination or adulteration with bacteria or any other extraneous matter.

The U. S. Pharmacopoeia has, for some time, been accepted as the standard authority for pure drugs. With the passage of the law it became the duty of the Revision Committee of the Pharmacopoeia to set up standards for these sterile surgical supplies. An advisory board

Editorial

Sterile Surgical Supplies

FIFTEEN years ago five patients, operated upon in a single week in a certain New York hospital, died of operative wound infections all of the same general character. From the last case of this series a spore-forming organism of the gas gangrene group was cultivated. It was found to be extremely pathogenic for several species of laboratory animals and produced a powerful specific toxin. The same species of organism was cultivated from two specimens of catgut of the same batch as that used in all of these operations. This seemed to prove beyond peradventure of a doubt that the catgut had not been sterilized and that the catgut was responsible for the infections.

This led to a comprehensive study of the problem of catgut sterility. Raw catgut is contaminated with pathogenic intestinal bacteria which must be killed before it is safe to use as suture material. A survey was made of specimens of catgut purchased on the open market. Twelve and one-half per cent of 174 specimens distributed by seventeen different firms and purchased in eleven different states were found to be contaminated with spore-forming organisms. Seven out of seventeen firms were implicated.

A test for sterility was devised to detect the presence of the most fastidious anaerobe imbedded in any size of catgut preserved in any kind of suspending fluid if it has not been destroyed in the sterilizing process. It is not feasible for surgeons and it should not be necessary for hospitals to test the sterility of the catgut which they use. The responsibility lies with the manufacturers of the product. It is obvious that, if every catgut firm subjected specimens from every sterilizing batch of catgut to such a sterility test before releasing the catgut for sale, it would hardly be possible for hospitals or doctors to purchase and use any unsterile catgut.

How could catgut firms be made to test their product and store it long enough to be sure of its sterility before offering it for sale? The only practical proposal which was made to accomplish this feat was to set up a reliable Control. Specimens of catgut would have to be purchased on the open market and be tested in some laboratory according to the sterility test devised. The Control should then immediately stop the further distribution of any faulty material. This would mean confiscating all of the unsterile batch and making it known to the surgical profession that the product was unreliable.

The Bureau of Standards was asked to undertake such a control but refused to do so. In like manner the National Institute of Health was

Review of Recent Meetings

REVIEW OF THE TWENTY-THIRD MEETING OF THE AMERICAN SOCIETY FOR THORACIC SURGERY, CLEVELAND, OHIO, JUNE 6, 7, AND 8, 1940

N. LOGAN LEVEN, M.D., ST. PAUL, MINN.

(From the Department of Surgery, University of Minnesota)

ON JUNE 6 the program was arranged as a joint session of the American Association for Thoracic Surgery and the National Tuberculosis Association.

Andre Cournand, D. W. Richards, Jr., and Herbert C. Maier, New York City: **Forms of Pulmonary Insufficiency Associated With Collapse Therapy.**—In patients with physical disability due to disease of the lungs or restriction of breathing apparatus, three general forms of insufficiency can be recognized: (1) failure of pulmonary ventilation, leading primarily to dyspnea (ventilatory insufficiency); (2) failure of respiratory gas exchange, leading to anoxemia and cyanosis (respiratory insufficiency); (3) combined failure of ventilorespiratory and of cardiocirculatory mechanisms, with variable symptomatology. Two cases are presented which illustrate different aspects of ventilatory, respiratory, and circulatory insufficiency associated with collapse therapy.

G. G. Ornstein, New York City, suggested a simple test for a surgical margin of safety; namely, if the maximum minute ventilation is six times the resting ventilation, surgery is safe. Max Pinner, Ithaca, N. Y., pointed out that the minute ventilation was important in reference to surgery depending on the distribution between both lungs. He stated that diaphragmatic paralysis produced the lowest breathing reserves, lowered the oxygen concentration, and increased latent pulmonary congestion; and that post-thoracoplasty scoliosis did diminish breathing reserves but did not produce respiratory insufficiency or cardiorespiratory impairment.

E. P. Eglee, R. H. Wylie (by invitation), and Adrian V. S. Lambert, New York City: **Empyema and Unexpanded Lung Problems in Pneumothorax.**—A report of a series of empyemas in the course of pneumothorax met with at Bellevue Hospital and in the Bellevue Clinic during the past five or ten years is presented. One hundred and thirty-six cases, or 7.8 per cent of all pneumothorax cases, developed empyema; the criterion for empyema being "thick pus" and not merely turbid fluid. The treatment consisted of drainage of the empyema by thoracotomy to reduce the surface of infection followed by thoracoplasty and later a Schede operation.

Louis Davidson, New York City, pointed out that two-thirds of these empyemas have a bronchopleural fistula and that this type of case when promptly treated as outlined offered 68 per cent cures. All thoracotomy patients not followed by thoracoplasty die. Jerome R. Head, Chicago, stated that most cases of empyema compli-

was selected to help in establishing these standards. This Board is composed of Dr. George McCoy, Dr. Harrison, of the National Institute of Health, and Dr. Louis Gershenfeld, of Philadelphia, with Dr. Arthur Shipley and myself representing the surgical profession. The Board has met on numerous occasions with representatives of the Bureau of Standards, the Food and Drugs Administration, the Army and Navy supply officers, and other government experts as well as with representatives of the manufacturers. Last year standards were set up for catgut and for absorbent cotton. Also a test for the sterility of all solid goods was established based on the sterility test which had been developed for catgut. These standards were incorporated into the supplement of the eleventh decennial revision of the Pharmacopoeia, which was published on Jan. 1, 1940, and will go into effect on Jan. 1, 1940. On that date the Food and Drugs Administration began its control over sterile surgical supplies. The manufacturers of these products will soon have to check the sterility of all of their sterile goods and strictly conform to the standards or risk the confiscation of these goods and court action. It is hoped that these measures will effectively banish unsterile catgut and other harmful surgical supplies from the market and that the surgical profession may purchase and use these goods with absolute confidence that they are working with sterile material and not running the risk of infection by their use. Thus will the labors of fifteen years be amply rewarded.

While the establishment of this control is the culmination of fifteen years of effort, we do not feel that this is to be the end of our labors. The standards which have been set up are not complete. For example the qualities of catgut next most important to sterility, which is an absolute requirement, are tensile strength and absorbability. Standards have been set up for tensile strength, but we expect the manufacturers to improve this quality and compete with one another in this effort. If we can get stronger catgut, we may employ finer sizes to do the same work we are now asking large sizes to do. When this is done we will undoubtedly want to raise the standard of tensile strength. With regard to absorbability the material available shows the greatest possible diversity. Some catgut firms have been putting out what they call ten-, twenty-, or forty-day chromic catgut, but when we asked them just what these figures meant some claimed that these sutures would hold tissues together for that length of time while others said that they meant the suture would resist complete digestion for that length of time, which is quite a different matter. Other firms contented themselves with the terms soft, medium, and hard to indicate the degree of tanning or chromicizing. It has been impossible to devise animal tests for catgut absorbability which duplicate conditions in the human body because so many factors are involved; for example, the tension of the sutures, the various tissues in which they are placed, and

Oscar Auerbach and Henry Green, Staten Island, N. Y.: **The Pathology of Cavity Healing.**—This study based essentially on post-mortem material is qualitative and directed at the methods of cavity healing rather than quantitative in the sense of establishing a frequency of healing. Those cases in which the cavities undergo healing and death occurs as a result of the complications of chronic pulmonary tuberculosis as amyloid uremia, mixed infection empyema, or some cause other than tuberculosis have been included in this report. Cavities were regarded as closed clinically when the sputum became negative and serial x-rays failed to reveal a preexisting cavity. Healing of the tuberculous cavity occurred in two ways: (1) The lumen of the cavity was obliterated ("closed" healing) and (2) the lumen of the cavity remained patent ("open" healing). Closed healing results either in the replacement of the cavity by a scar or the retention or inspissation of caseated material within the cavity, thus filling and obliterating its lumen. The junction with the bronchus closes and the wall of the cavity closes concentrically with calcification. Healing with an open cavity lumen or open healing may occur in the presence of draining bronchi which open widely into the lumen of the cavity. Two factors occur in this form of healing: first, the complete shedding of the inner zone of caseation, resulting in disappearance of tubercle bacilli from the sputum; and, second, the transformation of the tuberculous granulation tissue of the cavity wall into a nonspecific fibrous tissue. These two processes probably go on simultaneously. Cavity drainage by means of the Monaldi operation may permit more rapid healing of the cavity.

Max Pinner, Ithaca, N. Y., states that these cases of closed healing did not actually represent healed cavities but were only "cold abscesses." H. C. Sweeney, Chicago, stated that many people with tuberculous cavities that have healed died years later and the scar was overlooked.

Harold Brunn, Sidney Shipman, and Alfred Goldman (by invitation), San Francisco: **Intracavitation Studies in Tuberculosis.**—Pressure studies, examinations with the cavernoscope, and also bacteriologic studies of cavities as well as bronchoscopic examinations to determine the character of the bronchi were made. A method of study of cavities following somewhat that of Monaldi in Italy was presented. It was pointed out that the high tension in some cavities may account for some failures of collapse of cavities by thoracoplasty and decompression by needle or tube was suggested.

Leo Bloesser, San Francisco: **Further Experiences With Blocked Cavities in Pulmonary Tuberculosis.**—Manometric measurements by needling the cavity, the effect of pneumothorax on cavities, and the effect of inspiration and expiration and various postures on the shape and size of the cavity as seen in x-ray were studied. It was pointed out that collapse is theoretically wrong in blocked cavities and in these cases needling and aspiration of the cavity is advisable just prior to thoracoplasty.

Edward Kupka and Edwin Bennett, Olive View, Calif.: **Suction Aspiration of Tuberculous Cavities (the Monaldi Procedure).**—Closed cavity drainage has been limited to needling in connection with cavity research until its elevation by Monaldi into an important therapeutic measure. In 1938 he first employed continuous or intermittent suction over a prolonged period through a catheter draining the cavity. If disease changes in the parenchyma about the cavity have not progressed too far, the suction acts in several ways: (1) initially, drainage of cavity contents, such as pus, blood, detritus, and bacilli; (2) re-expansion of surrounding atelectasis; (3) reeration of surrounding areas of exudative infiltration;

ing pneumothorax can be cured by conservative treatment if there is not too much contralateral disease. Daily irrigations with antiseptic solutions are used to sterilize the cavity, avoiding drainage and then performing a simple thoracoplasty. A. V. Lambert, New York City, pointed out that pneumothorax should not be taken lightly. Too often it meant giving a disease to the patient because of poor technique or too prolonged utilization of pneumothorax. He stated that cases of tuberculous empyema were treated too long medically before coming to surgery.

B. P. Potter, Jersey City, N. J.: Hospital Mortality and Life Expectancy of Two Groups of Patients Treated With and Without Collapse Therapy.—A comparison was made of two groups of patients: the first during the period between 1926 and 1932, when 6.2 per cent received collapse therapy; the second group treated in the interval between 1932 and 1938, when 61.2 per cent of the admissions were subjected to one or a combination of the procedures of pneumothorax, phrenic interruption, and thoracoplasty. The comparison of the total annual death rate and death rate per new admission in the two periods indicates a definite reduction in the total and per new admission death rate in the later years.

Jerome R. Head, Chicago, felt that the improvement since 1925 was not all due to collapse therapy but to some extent due to more strict rest regimen.

Minas Joannides, Chicago, stated that collapse therapy decreased the morbidity and also the risk of contact by augmenting the frequency of sputum conversion and causing the disappearance of cavities. He pointed out that the improvement of the patient and the death rate varied directly as did the time in the course of the disease at which the patient presented himself.

R. G. Bloch, W. B. Tucker (by invitation), and W. E. Adams, Chicago: Standards and Criteria in Artificial Pneumothorax Therapy.—This paper pointed out that in the management of the tuberculous patient some use pneumothorax universally; whereas, certain indications should be observed. Collapse therapy demands the presence of a cavity and should not be used in noncaseous, nonexcavated lesions. Of paramount importance is the combination of artificial pneumothorax with carefully supervised rest treatment. Sanitarium treatment and teaching are necessary for the patient. Ambulatory pneumothorax is not advised. The manner in which the overwhelming number of reports on results of artificial pneumothorax treatments have been made in the literature is largely responsible for an overenthusiasm as to its possibilities in curing tuberculosis. Few reports are based on the cognizance of the fact that the successful treatment means: (a) restoration of the lung to its physiologic function, i.e., complete re-expansion; (b) adequate roentgenologic evidence of healing of the tuberculous involvement, especially of the disappearance of cavities; (c) return of the patient to normal life, with (d) persistent absence of tubercle bacilli in the sputum; (e) persistent absence of all symptoms of activity; and (f) complete disappearance of all extrapulmonary complications.

Only after at least two years of satisfactory application of these criteria should a patient be considered as cured by the treatment. A distinct line is to be drawn between such final results and initial symptomatic improvement which is frequent and striking but also often misleading as to the ultimate outcome. The application of stricter standards in judging final results tends to reduce the percentage of "cures" considerably.

In the discussion D. B. Cole, Richmond, Va., stated that he found ambulatory pneumothorax satisfactory in many cases and that he thought it was important to get the patient back to work.

John S. Harter and Allen A. Lilienthal (by invitation), Sanatorium, Miss.: **Extrapleural Pneumonolysis in Artificial Pneumothorax. A Report of 28 Cases.**—This series of cases included pneumothoraces which were not effective due to adhesions, the adhesions being of the type that could not be severed by the closed method or the open method of pneumonolysis. The parietal pleura was separated from the chest wall in the region of the adhesion and the pleura opened and cut around so as to leave parietal pleura attached to the free adhesions. The removal of the pleura around the adhesions transforms a small extrapleural pneumothorax into a complete intrapleural pneumothorax. In twenty-eight cases operated upon an effective pneumothorax was obtained in twenty-seven.

E. J. O'Brien, Detroit, felt that in most cases a thoracoplasty would be of more value than this type of procedure. Minas Joannides, Chicago, presented a motion picture of an axillary approach for this operation, pointing out that from the axillary approach one could work either anteriorly or posteriorly.

William A. Zavod (by invitation), New York City: **Bronchospirography. 1. A New Bronchospirographic Catheter and the Technique of Intubation.**—A double-channelled rubber catheter for intrabronchial intubation was described. The channel for the trachea was 9 cm. shorter than the channel for the bronchus and each channel had an inflatable bag which permitted separate respiration of each lung. Under local anesthesia the catheter was passed into the trachea and the left main bronchus. By inflation of the bronchial and tracheal bags studies could be made on each lung separately. This catheter is a modification of the Gebauer tube presented at a previous meeting.

George Leiner (by invitation), Max Pinner, Ithaca, N. Y., and William Zavod (by invitation), New York City: **Bronchospirography. 2. Application to Collapse Therapy.**—In a series of bronchospirographic observations made on patients with pulmonary tuberculosis it was found that neither clinical nor roentgenological findings are reliable indices of the functional capacity of the lung. It was found that collapse therapy might reduce the pulmonary ventilation without decreasing the oxygen consumption, indicating a better economy by compression of the diseased tissue only. Thus, there might be an increase of the ventilating efficiency in spite of a reduction in vital capacity. The authors felt vital capacities were entirely misleading and that bronchospirographic studies should be made in all cases before any irreversible collapse procedure was carried out.

S. O. Freedlander, Cleveland, stated that, in general, clinical and x-ray evidence parallels the bronchospirographic findings and that, while these findings might be decisive in an occasional case, the procedure would not become routine in estimating the surgical risk prior to collapse therapy.

David Salkin and A. V. Cadden (by invitation), Hopemont, W. Va.: **Rest and Collapse in Pulmonary Tuberculosis.**—This paper proposed a new classification of pulmonary tuberculosis. In using this proposed system a series of cases was studied to evaluate three different programs of therapy: (1) mild activity, (2) strict bed rest, (3) collapse therapy. The use of strict bed rest as a standard by which to measure other forms of treatment was suggested.

Emil Bogen (by invitation), Olive View, Calif., pointed out that collapse therapy produced a higher mortality than rest in minimal cases but that in advanced cases collapse therapy reduced the fatality rate.

A. V. S. Lambert, New York City: **Presidential Address. Etiology of Thin-Walled Cysts Occurring Within the Thorax.**—Intrathoracic cysts were divided

(4) compensatory expansion (emphysema) of normal pulmonary tissue within a contiguous area; (5) finally, holding of cavity walls in close apposition until symphysis takes place. An open or potentially open pneumothorax space is an absolute contraindication to cavity puncture because of the danger of empyema. To seal the pleural surfaces together, single or repeated injections are made of the patient's own blood into the pleural space, until repeated pneumothorax attempts over the area to be punctured with the trocar fail to elicit manometer fluctuations.

A tube is inserted and attached to intermittent suction with a trap for secretions. Treatment is continued until the cavity is closed and the catheter spontaneously extrudes with an upper limit of four to six months. Isolated balloon type cavities between 3 and 8 cm. in diameter lying in the subclavicular area with little surrounding parenchymal involvement offer the most favorable indication. In some instances closed cavity drainage may be used preparatory to thoracoplasty since cavities may reduce in size, sputum become negative, and the general condition improve to a point where the major procedure can be done. A series of twenty-five cases was reported, the majority of which were still under suction.

In the discussion of this paper G. G. Ornstein, New York City, felt that the indications for the Monaldi operation were: (1) a giant ball-valve cavity; (2) bilateral disease; (3) marked decrease in pulmonary ventilation. W. A. Hudson, Detroit, stated that the Monaldi operation was of value in patients where thoracoplasty failed. It removed the secretion and prepared the patient for further surgery. In addition to drainage Hudson irrigates the cavity with a digestant aiding in the removal of slough and tuberculous granulation tissue.

David T. Smith, Durham, N. C.: Treatment of Fungus Infections of the Lung.—Many pathogenic fungi produce diseases in man which have a higher mortality than tuberculosis. In the treatment of fungus infection of the lung Smith indicated the value of iodides in actinomyces, of gentian violet in pulmonary infection with monilia, of colloidal copper or antimony and potassium tartrate in cases of coccidioidal granuloma. He felt that sulfanilamide had proved to be of some value in the treatment of actinomyces.

In discussion O. H. Wangenstein, Minneapolis, Minn., pointed out that actinomyces might be endogenous or exogenous and that the actinomyces of the mouth resembled the others. Since the actinomyces is anaerobic, nonmotile, and carried by macrophages, he recommended simple eurement of the lesion, removal of the dead tissue, and exposure of the lesion to the air, indicating this as the major factor in the therapy of this disease.

Meetings on June 7 and 8 were then held in the auditorium of the Medical Library Association.

E. C. Janes and (by invitation) D. B. Aitchison and A. Forsberg, Hamilton, Ontario: Extrapleural Pneumonolysis.—This paper was based on the study of seventy-seven cases. There were eight deaths and in two-thirds of the cases there was closure of the cavity with sputum conversion. One-fourth of the cases had poor results and required later thoracoplasty. Fifteen cases were converted to oleothorax to maintain permanent collapse of the lung. Special reference was made to irrigation with Dakin solution of the extrapleural space prior to closing to avoid clotting with subsequent obliteration and secondary infection. This procedure is indicated where urgent collapse is necessary to control bleeding, where there is bilateral disease, and in young patients. It may also be useful to prepare a very ill patient for more drastic surgery. The presence of a large cavity close to the periphery, extrapulmonary disease, and low vital capacity are contraindications to this procedure.

therapy did no good in bacterial endocarditis and that no cures have been reported since 1924. In these otherwise hopeless cases this operation should be tried.

Frederick R. Mautz, Cleveland, Ohio: Mechanism for Intermittent Pulmonary Insufflation in Thoracic Surgery.—A respirator built into a gas machine for intermittent pulmonary ventilation was demonstrated. Intermittent pressure is more efficient in open pneumothorax than the continuous flow mechanism. This machine gives perfect control of an open pneumothorax because it is visibly adjustable.

Claude S. Beck, Cleveland, Ohio: Exhibit of Experimental Work on the Heart.—A specimen was demonstrated by slides to show definite collateral circulation of the coronary with the internal mammary arteries, after ligation of the coronary arteries and transplantation of a muscle fat graft in the experimental animal.

Harold Feil, Cleveland, presented a follow-up study of 30 cases of coronary sclerosis operated upon by Beck, following these over a period of from five years to three months after operation. In this series there were twenty-nine men and one woman of an average age of 51 years. All of these patients had failed to respond to medical treatment, which consisted chiefly of administration of nitroglycerin and aminophyllin. While there was no immediate operative mortality, ten patients died in the period a few hours to a few months following the operation, giving a 33 per cent mortality. Of the patients surviving operation an excellent result was obtained in ten; that is, the patients were able to return to work; in seven the result was considered fair, the patients having moderate pain relief, and in three there was no relief of pain. There may be relief of pain and the weakness may continue. **J. W. Strieder, Boston, presented a case of coronary sclerosis that was improved six months following an omental graft after the method of O'Shaughnessy.** Gastric symptoms developed at that time due to a hiatus hernia of the stomach through the site of the transplant of the omentum. The patient died forty-five minutes after the reduction of this hernia at operation. A rich vascular supply was found present between the omentum and the heart.

A. L. Brown (by invitation), San Francisco, demonstrated a modification of the Jackson bronchoscope. Light was transmitted to the end of the bronchoscope through a lucite carrier. By this method a slightly larger working space was obtained in larger tubes. The possibility of diversion of the light in any direction from the end of the lucite might prove to be of some advantage.

W. H. Stewart, H. C. Maier, C. W. Breimer (by invitation), New York City: Ciné-Roentgenographic Studies of the Pulmonary Circulation, the Chambers of the Heart, and the Greater Blood Vessels, in Health and Disease.—By the rapid injection of diodrast into the veins, very interesting motion pictures were made of the pulmonary circulation, chambers of the heart, and greater blood vessels. The possibility of use with this method in diagnosis was pointed out.

Brian Blades, St. Louis: Individual Ligation Technique for Lower Lobe Lobectomy.—A technique involving separate ligation of each anatomical structure in the hilum of the lung is recommended for lower lobe lobectomy. The method is based on investigations of the surgical anatomy of the lower lobes and experiences with eleven successful cases in which the procedure was employed. Using this method a higher incidence of permanent bronchial closure was obtained and a decrease in the number of empyemas was found. In eleven cases five did not have empyema and six had empyema but not the putrid type. Five of these had

into three groups: parasitic, dermoid, and lymphangiomas. These lymphatic cysts probably arise as diverticuli from the pericardiocoelom by failure of the pericardial lacunae to fuse. They should be called pericardiocoelomic cysts. These cysts are usually discovered by x-ray and should be removed before pressure symptoms arise. They are thin-walled cysts lying anterior to the pericardium and lingula and may be shelled out clean by blunt dissection. They appear to lack any blood supply.

Peter Heinbecker, St. Louis: Angina Pectoris.—A general review of the mechanism of painful sensations and in particular those arising in the heart was presented. Whereas pain endings in the skin are easily excited by any stimuli, those in the viscera are excited by tension and tissue metabolites. Ischemia of cardiac muscles due to occlusive arterial disease will produce metabolites which stimulate pain endings. Muscular effort and anoxemia increase production of metabolites and similarly produce stimuli. The pathways of the pain were traced. This cardiac pain is helped by the usual rest, vasodilator drugs, and morphine. Although total ablation of the thyroid reduces the work of the heart, it also tends to increase arterial degeneration and three-fourths of these cases die of rupture of the aorta. Alcohol injections of the ganglia or excision of the inferior cervical and first and second thoracic ganglia offer some relief of the pain. Establishment of collateral circulation to the heart by muscle or omental transplants to the heart or by the establishment of an adhesive pericarditis has shown encouraging results.

Claude S. Beck, Cleveland, Ohio, pointed out that neither metabolites nor anoxemia alone would produce cardiac pain, but together they would increase the pain, one augmenting the other. While general anoxemia was well tolerated, local anoxemia was devastating to the heart. Experimentally, he found that simultaneous cervical sympathectomy with ligation of the left coronary artery reduced the mortality from 80 to 50 per cent, but that cervical sympathectomy sixteen days after ligation of the arteries offered no protection.

Arthur S. W. Touroff, New York City: The Surgical Treatment of Patent Ductus Arteriosus Complicated by Subacute Bacterial Endocarditis.—Subacute bacterial endocarditis is readily superimposed in cases of patent ductus arteriosus. The infection is chiefly in the left side of the heart on account of the higher oxygen content which allows better growth of the *Streptococcus viridans*. Thus, excision of the patent ductus may remove a focus of infection and decrease the infection in the pulmonary artery by reducing the oxygen tension. Operation in these cases is complicated because of the fact that the periarteritis usually makes the ductus adherent to the pulmonary artery. This, together with degenerative atheromatous plaques, makes the ductus friable. Four cases were reported; one patient has been free from all evidence of the original lesions for more than three months; two died of hemorrhage and the fourth was improved.

Frank S. Dolley, Los Angeles, indicated that the risk of postponing operation in cases of patent ductus arteriosus was greater than the risk of operation due to the probability of the development of subacute bacterial endocarditis. However, he felt that operation in cases of subacute bacterial endocarditis was of doubtful value since, as a rule, the infection had extended into the conus. He advocated early operation before vegetations formed and presented nine cases of children who were well following ligation of a patent ductus arteriosus. In none of these was infection present at the time of operation. **J. W. Strieder, Boston,** said that chemo-

Evarts Graham, St. Louis, pointed out that, if the chest wall is not collapsed by thoracoplasty, a load is put on the opposite lung by a lobectomy.

Leo Eloesser, San Francisco, found thoracoplasty disappointing in cases of bronchostenosis and pulmonary suppuration and preferred either drainage or lobectomy in these cases. He advised lower lobe lobectomy for bronchiectasis that developed after upper lobe thoracoplasty and indicated that most of these cases of bronchiectasis were probably not due to tuberculosis.

J. J. Longacre and Ralph Johanson (by invitation), Cincinnati, Ohio: **An Experimental Study of the Fate of the Remaining Lung Following Total Pneumonectomy.**—Hyperplastic regeneration of the remaining lung following total removal of one lung occurs in young animals in contrast to the dilatation of the definite lobules occurring in adult animals. Following pneumonectomy, the cardiorespiratory reserve is cut in half, sufficient for rest and moderate exercise but inadequate when these animals are subjected to strain. In nine to twelve months the cardiorespiratory reserve returns to 70 or 80 per cent of normal in the adult animals; whereas, in animals pneumonectomized as puppies the return is 100 per cent, showing that capacity of the organism for further growth accounts for the difference in the anatomical changes and also the difference in function. In animals pneumonectomized as adults there was noted dilatation of the atria and the alveoli at the periphery of the lung with some breaking of alveoli and elastic fibers causing emphysema. It was pointed out that thoracoplasty might prevent this dilatation in human beings subjected to pneumonectomies.

Evarts Graham, St. Louis, indicated that thoracoplasty in cases of pneumonectomy would prevent kinking of the great vessels and the trachea to relieve discomfort and dyspnea. W. E. Adams, Chicago, studied the effect of paralysis of the diaphragm and thoracoplasty in animals having lobectomies and pneumonectomies. He found that there was less dyspnea in cases with section of the phrenic nerve. In one animal with both diaphragms paralyzed and bilateral lung resection, leaving but one lobe, he found a normal reaction to conditions simulating an ascent to 27,000 feet altitude. The animal did not lose consciousness.

Chevalier L. Jackson and A. R. Judd (by invitation), Philadelphia: **The Role of Bronchoscopy in the Treatment of Pulmonary Abscess.**—The causes of lung abscess and the bacteriology of these abscesses were reviewed in a series of 137 cases. The role of bronchoscopy during several stages of lung abscess was indicated. First, as a prophylactic measure lung abscess may be prevented by aspiration of material from the bronchus. Second, as a diagnostic measure bronchoscopy may aid in the differentiation of a tuberculous cavity by obtaining material for bacteriologic study and also may identify a tumor in the bronchus as an etiologic agent. Third, during the acute stage bronchoscopic drainage may lead to spontaneous healing. It is emphasized, however, that bronchoscopic and so-called nonsurgical treatment should not be carried beyond the optimum time for the employment of some other procedure such as surgery. P. C. Samson, Oakland, Calif., stated that next to cancer lung abscess was the most fatal common disease in the chest. He advised bronchoscopic examination of all cases except those complicated by hemorrhage or brain abscess. If improvement does not occur within a few days, surgical treatment should be used. The more chronic and the more putrid the abscess, the less likely it is to improve by bronchoscopic drainage.

Paul W. Gebauer, Cleveland, Ohio: **The Differentiation of Bronchiogenic Carcinomas.**—Pathologically and clinically small-cell carcinoma, adenocarcinoma and squamous-cell carcinoma are the three fundamental types of bronchogenic

a small bronchial fistula as demonstrated by saline injection. However, this did not prolong the hospital stay. In these cases an average hospital stay was thirty days. By the individual ligation technique the danger of compression or encroachment on the middle and upper lobe bronchi that occasionally obtains when mass ligation of the lobe or hilum is carried out may be avoided.

Harold Brunn, San Francisco, pointed out that mass ligation of the lobe or hilum was not clean surgery and that, if the condition of the patient permitted, the individual ligation technique should be used. He felt that formation of adhesions to the upper lobe as a preliminary procedure to the operation made the post-operative course easier. R. M. Janes, Toronto, Ontario, pointed out that failure of the middle and upper lobes to expand after lower lobe lobectomy may be accounted for by encroachment on these bronchi occurring when mass ligation of the hilum is used.

J. J. Singer, John C. Jones, and L. J. Tragerman (by invitation), Los Angeles: Aseptic Pleural Adhesions Experimentally Produced.—In this study by injecting various substances in the pleural spaces of rabbits aseptic adhesions were successfully produced. The best results were obtained using iodized tale in saline solution. By this method the saline was readily absorbed and left an even deposit of talc. The adhesions produced were particularly effective in the fixation of the mediastinum which represents the most vulnerable area of infection following lobectomy. It was pointed out that the risk of thoracic surgery is reduced by the preliminary treatment of the pleura by this method.

Clarence Bird, Louisville, Ky., injecting silicon into the pleural cavity, found that more effective adhesions were formed if a phrenicectomy had been performed and if the pleural cavity was kept dry. Cameron Haight, Ann Arbor, Mich., used iodized tale to make adhesions prior to lobectomy. He advised using a minimum amount of the powder, just sufficient to produce a sheen over the surface. If too much powder is used, it collects in masses. L. J. Tragerman, Los Angeles, indicated that the adhesions probably were not as important as the inflammatory blocking of the lymphatics.

Frank S. Dolley and John Jones, Los Angeles: Experiences With Lobectomy and Pneumonectomy in Pulmonary Tuberculosis.—In this paper seven cases were reported, four total pneumonectomies and three lobectomies. Of the four cases of pneumonectomy two are dead and two are dying with contralateral spread, while the three cases of lobectomy are still alive and well. Preliminary thoracoplasty with apicolysis was advised to improve the preoperative condition. Thoracoplasty also obviates the need for obliteration of the dead space following pneumonectomy or lobectomy. Individual ligation of the hilus, catheter suction of the trachea, and minimal handling of the lung were advised. If the lung is adherent, ligation of the hilus should be done as the first step to prevent contralateral spread by inoculation of the infection. It is important to make the patient cough post-operatively to get rid of secretions.

John Alexander, Ann Arbor, Mich., reported cases of bronchostenosis treated by thoracoplasty with good results. He pointed out that in some cases the stenosis might be so small that a preliminary thoracoplasty prior to lobectomy would be dangerous. If ulcerative tracheobronchitis due to tuberculosis cannot be entirely removed by this operation, it is contraindicated. He reported one pneumonectomy and two lobectomies for tuberculosis which apparently are cured.

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Paul W. Gebauer, Cleveland, Ohio: **The Differentiation of Bronchiogenic Carcinomas.**—Pathologically and clinically small-cell carcinoma, adenocarcinoma and squamous-cell carcinoma are the three fundamental types of bronchogenic

cancer. The differences of these types early in the course of the disease sometimes permit their distinction by combined clinical, radiologic, and bronchoscopic investigations. Late in the disease this is true in approximately 60 per cent of cases. Bronchoscopy will be negative in 40 or 50 per cent of cases if performed at the onset of symptoms. When negative, it should be supplemented by other biologic, endoscopic, and radiographic diagnostic methods until the cause for symptoms is known. The impression that clinical symptoms tend to occur early, when the tumor is in an operable state, has been gained from this study. Therefore, it is felt that if the diagnosis is made early and there is the proper selection of operative material, surgical treatment will gain a respectable position in therapeutics.

Evarts Graham, St. Louis, in discussion, stated that squamous-cell carcinomas of the bronchi are a definite group, but it is impossible to differentiate the small-cell carcinomas and adenocarcinomas, since these varied depending on the portion of the tumor examined. Small-cell carcinomas, adenocarcinomas, and the adenomas probably arise from remnants of fetal bronchial buds. The adenomas, he said, were potentially malignant and should not be removed locally. Alfred Goldman, San Francisco, found one case in fifty adenomas that metastasized; fifteen cases having a fifteen-year history showed no evidence of metastasis, the growth being by local extension.

Henry K. Beecher (by invitation), Boston: **Controversial Points in Anesthesia for Thoracic Surgery.**—Of the anesthetic agents, Beecher advised using ether since it could be used with 96 per cent oxygen; whereas, cyclopropane was used with 75 per cent oxygen. Cyclopropane may be toxic to cells, interfering with oxygen use. Toxic cardiac effects are noticed after the use of cyclopropane for one hour; the pulse rate increases and the blood pressure drops. Ether is well tolerated with circulatory impairment and that it is irritating is of no importance since it does not affect the mortality or morbidity in his experience. The objections to spinal anesthesia were the (1) inability to aspirate secretions from the trachea, (2) inability to give positive pressure effectively, (3) tendency to suppress cough, and (4) greater mortality with its use. In many cases an intratracheal tube is important because it offers an open airway for positive pressure and for aspiration of sputum. He felt that it was contraindicated in cases of pulmonary tuberculosis. Endobronchial catheters in anesthesia offer technical difficulties and may come out at inopportune times. The inflatable cuff on intratracheal catheters was criticized as unnecessary and in the presence of a gush of pus or blood might cause spillage of contents into the other side, which otherwise would come up alongside the tube. Mechanisms for controlled respirations were considered inadvisable and unnecessary.

H. R. Decker, Pittsburgh, stressed the use of local anesthesia supplemented by cyclopropane or by sodium pentothal. He avoided the use of ether in cases of pulmonary tuberculosis. G. E. Lindskog, New Haven, Conn., favored the use of avertin and intratracheal cyclopropane, using nitrous oxide anesthesia if local anesthesia alone was inadequate when cautery was to be used. He pointed out that ether was explosive if there was a high oxygen content in the mixture.

Howard K. Gray and I. C. Skinner (by invitation), Rochester, Minn.: **The Operative Treatment of Cardiospasm.**—In over 1,200 cases of cardiospasm seen at the Mayo Clinic, operations for the relief of cardiospasm were performed only seven times. These cases were reported. Mikulicz' operation of manual dilatation of the cardia was performed four times, esophagogastrostomy one time, thoracocervical sympathectomy one time, and abdominal sympathectomy com-

bined with manual dilatation of the cardia one time. In cases in which the esophagus is markedly dilated, lengthened, and tortuous (sigmoid esophagus) with the development of a reservoir below the opening of the cardia, surgery at times will be found necessary. The technique of abdominal esophagogastrostomy was illustrated and the case reported.

H. J. Moersch, Rochester, Minn.: The Injection Treatment of Esophageal Varices.—A case of esophageal varices successfully injected with a sclerosing solution through an esophagoscope was reported. A review of the various treatments used for esophageal varices was presented. Since fatal gastrointestinal hemorrhage occurs in 80 per cent of all esophageal varices and 50 per cent of all cases of cirrhosis of the liver die of hemorrhage, some method of therapy in these cases is highly desirable.

Alton Ochsner and (by invitation) Michael Debakey and Samuel Murray, New Orleans, La.: Surgical Aspects of Carcinoma of the Esophagus.—Three cases of carcinoma of the esophagus operated upon by the authors were reported. One patient with carcinoma of the esophagus in whom an excision of the lesion and an esophagogastrostomy was performed lived over one year with no evidence of recurrence. A transthoracic approach was used removing the left eighth rib, crushing the phrenic nerve and opening the diaphragm. A wide resection of the stomach was carried out. The most desirable procedures for lesions at various levels in the esophagus were considered and illustrated.

B. Noland Carter and (by invitation) Jean Stevenson and Osler Abbott, Cincinnati, Ohio: Esophagogastrostomy. An Experimental Study.—Two successful cases of esophagogastrostomy were reported. Clinically the chief danger of esophagogastrostomy is leakage at the line of suture and this is most commonly due to tension. A method to obviate tension on the anastomosis has been devised. This consists of anchoring both the stomach and the esophagus to the periosteum of nearby ribs and vertebral bodies. A second complication of stricture at the site of an anastomosis may be avoided by making the anastomosis to a circular hole in the stomach. This was indicated by experimental work.

Book Reviews

A Manual of Otology, Rhinology, and Laryngology. By Howard C. Ballenger, Assistant Professor of Otolaryngology, Northwestern University School of Medicine. Pp. 302, with 90 illustrations and 4 color plates. Philadelphia, 1940, Lea and Febiger. \$3.75.

This manual is intended for the undergraduate medical student. It is a condensed version of the well-known Ballenger *Textbook on Diseases of the Nose, Throat and Ear*, the seventh edition of which appeared in 1938. Dr. Howard Ballenger was the junior author of that text which was written originally by Dr. William L. Ballenger.

The manual is a little less than one-third the length of the textbook. Its purpose is to emphasize anatomy, etiology, symptoms, and diagnosis. Surgical technique is omitted. A chapter on bronchoscopy which appeared in the textbook is entirely omitted.

The subject material is dealt with in four parts. The nose and accessory sinuses are treated in eleven chapters which are covered in 80 pages; the pharynx and fauces are covered in five chapters totaling 134 pages; diseases of the larynx receive six chapters of 34 pages; and the ear is treated in thirteen chapters of 121 pages.

There have been few manuals of this type available to undergraduate students. Consequently, this edition helps to supply a need. It is well written and illustrated and emphasizes the essentials which should be the basic part of undergraduate instruction.

Orthopedic Operations (Indications, Technique and End Results). By A. Steindler. Pp. 766, with 323 illustrations. Springfield, Ill., 1940, Charles C. Thomas, Publisher. \$9.

The book is divided into three portions. The first, on general biological and clinical topics pertaining to orthopedic operations, comprises 66 pages and includes 32 pages devoted to operative approaches to bones and joints. The second section of 305 pages is devoted to descriptions of the technique of various orthopedic operations and comprises twelve chapters. It includes surgery of tendons, fascial and ligamentous surgery, surgery of bones, joints and nerves, skin, and the spine. Amputations are included in the section on the surgery of bones.

The third section is devoted to the indications for specific operations and end results in various orthopedic conditions. This includes nine chapters which are devoted to congenital deformities, traumatic and constitutional deformities, inflammatory conditions, chronic arthritis, disturbances of the nervous system, degenerative bone diseases, tumors, and circulatory diseases.

The book is based on the experience of the author's clinic at the University of Iowa and in both the second and third portions statistics are given as to the results obtained in this clinic from many operative procedures. These results are classed as good, fair, and poor. In the third section similar statistics are given as to the results obtained by the operative treatment of specific conditions. These statistics represent a vast amount of looking up of histories and this work appears to have been done by the author's students and assistants. However, it is the reviewer's opinion that such bare statistics are of relatively little value.

In Section 3 reference is made to the operative procedures in Section 2. Unfortunately, in these references to the operative procedure the page is not given, but one is referred back to Part 2, Chapter X, etc., as the case might be, and it is troublesome to look up the operative technique. Likewise, in the description of the operative technique in Part 2 one is referred back to Part 1 for a description of the operative incision.

It is thus evident that this is not an extensive operative surgery, because, in attempting to cover both the operative technique and the indications for specific operations in the various orthopedic conditions, the author has devoted more than one-half of the book to the latter and has limited the part of the book on operative technique to approximately 300 pages. Naturally, many operations are omitted. In the preface the author states that this is not because these operations were not known to him, but because their validity did not impress itself sufficiently upon him. Most orthopedic surgeons will differ with any other orthopedic surgeon as to what operations are worthy of inclusion in a book, the title of which is *Orthopedic Operations*, because they all have their preferences.

The book is rather sparsely illustrated, there being 322 illustrations, of which only 100 are included in Part 2, which is devoted to operative technique. The illustrations in Part 2 are mostly original drawings and are clear and illustrate the point which they are intended to convey, although, for the most part, they are rather sketchy as to the anatomy of the region. The same is true of the description of the various operations. It is believed that in a book of this sort the technique of the various procedures should be described in detail and that the difficulties which may be encountered should be mentioned so that a competent surgeon may be in a position to perform a given operation after he has read its description. However, if the surgeon has the time and access to a good medical library he can look up the detailed description of the various procedures which are mentioned, because the value of the book is enhanced by a list of references which is placed at the end of each chapter.

On the whole this is a very valuable and full record of Dr. Steindler's work at Iowa City. For this reason it will be welcomed by American orthopedic surgeons.

Chronic Diseases of the Abdomen. A Diagnostic System. By C. Jennings Marshall. Cloth. Pp. 247, with 131 illustrations. Boston, 1939, Little Brown & Company. \$6.

This book of 247 pages presents a plan of study of the chronic diseases which occur within the abdomen, with a consideration of the symptomatology of diseases outside of the abdomen which must be differentiated from abdominal disease. The work is divided into two parts. Part I covers 48 pages and is devoted to methods of diagnosis. Differential diagnosis is considered in Part II, which fills the remainder of the book. The value of the book lies chiefly in the second part, although some important diagnostic methods are described in the first part. The differential diagnosis of chronic abdominal disease is approached with pain as the guiding symptom. At first the diseases which may cause general, vague, and midabdominal pain are considered. Following this the possibilities of disease in all sections of the abdomen and back are considered when pain is a symptom in each locality. All of these are thoroughly discussed.

At the end of the book several pages are devoted to signs and symptoms which may or may not be associated with pain. These are hematemesis, ascites, variations in appetite, loss of weight, jaundice, chronic diarrhea, hematuria, vomiting, pyrexia in abdominal disease, and abdominal tumor.

A differential diagnosis of any diseased condition cannot be made unless the possibilities are considered. In this book the possibilities are mentioned and are briefly or fully considered as the importance of the location of pain in the abdomen seems to warrant. This is a valuable book, logically arranged for teaching and a ready reference in the study of chronic abdominal disease.

Surgery of the Alimentary Tract. By Sir Hugh Devine. Cloth. Pp. 1,046, with 690 illustrations. Baltimore, 1940, Williams and Wilkins Co. \$15.

In this volume of more than 1,000 pages the author has not attempted to develop systematically the surgery of all the contents of the peritoneal cavity. His principal concerns have been the surgery of ulcers and of malignancies of the colon and rectum. He does describe, however, operative procedures upon the biliary tract, spleen, and other accessories to the alimentary tract proper.

The work is written in four parts. The basis of this division is by no means clear. Subdivision of the subject matter on a more consistent plan or along more orthodox lines would have made the book far more readable.

The special value of the work lies in the description of technical procedures to which the author has given obviously much time and thought. All surgeons having a keen interest in gastric or colonic surgery will find much of value in these pages, which are in essence a digest of Devine's experience. They will be somewhat disturbed to note that an analysis of the author's results, even in the chapters of his own special interests, is not contained in the volume.

The book can be recommended enthusiastically, not as a source book, nor even as an authoritative work of reference on surgery of the alimentary tract, but rather as the résumé of the experience of a surgeon, whose ideas and technical contributions to certain aspects of surgery of the alimentary tract are of the greatest interest.

An Introduction to Gastro-Enterology. By Walter C. Alvarez, M.D. Ed. 3. Cloth. Pp. 778, with 186 illustrations. New York, 1940, Paul B. Hoeber, Inc. \$10.

This book, published previously but under the title *Mechanics of the Digestive Tract*, appears now in enlarged form under the modest title of *An Introduction to Gastro-Enterology*. As the preface of the author indicates, the monograph is intended as a source book for various chapters of clinical physiology of the gastrointestinal canal. The admirable task which the author has set himself he discharges faithfully. Like earlier editions, it deals principally with the problems of motility of the gastrointestinal canal. It is in no sense a complete treatise on any of the common clinical disorders of the digestive tract. Yet, the writer, because of his experience as both investigator and clinician in the province of gastroenterology, has compounded a book that will be extremely useful for purposes of orientation to both physiologists and clinicians. The book concludes with an informative chapter on books of reference for various aspects of gastroenterology which the reader will welcome. A long and carefully selected bibliography is appended. The book can be recommended enthusiastically for the purpose for which its author intended it; namely, as an orientation source book for many chapters in physiological aspects of gastroenterology.

The Surgery of Injury and Plastic Repair Work. By Samuel Fomon, M.D. Cloth. Pp. 1,409, with 925 illustrations. Baltimore, 1939, Williams and Wilkins Co. \$15.

This is in many respects a remarkable book. The first 500 pages are devoted to the general considerations of operative technique, tissue transplantation, wounds, burns, fluid and electrolyte requirements of the surgical patient, shock, anesthesia and pre- and postoperative management. The remaining 900 pages deal with special chapters of what is commonly described as plastic surgery.

The general surgical consideration which precedes the accounts peculiar to reconstructive surgery in the various regions is particularly good and complete. This reviewer feels constrained to say it is the best account of surgical principles that he has found in a treatise dealing with a special province of surgery. If this book is a reflection of the plastic surgeon's interest in the general principles of surgery, one may ask with justification, is the plastic surgeon to become the general surgeon of tomorrow, entrusted with the responsibility of carrying on the traditions and teachings of general surgery?

The historical accounts in many of the chapters are unusually good and complete. This reviewer would have anticipated finding in a book of this standard of excellence a more complete discussion of the microscopic aspects of wound healing, including consideration of ligatures and strengths of the coaptated tissues at various phases in the healing period. The plastic procedures of genitourinary, gynecologic, intestinal, and orthopedic surgery are not described. A valid criticism which with all fairness may be leveled against the text is lack of uniformity in illustrations. Though the text is illustrated generously, in the main, the illustrations are not of the quality which one would anticipate finding in a text of plastic surgery.

A well-selected bibliography accompanies each chapter and a useful bibliography completes the text. The book may be recommended as a useful source book to both elementary and advanced students of surgery.

Fractures and Other Bone and Joint Injuries. By R. Watson-Jones, B.Sc., M.Ch., Orth., F.R.C.S. Cloth. Pp. 723, with 1,040 illustrations. Baltimore, 1940. Williams & Wilkins Co. \$13.50.

This book of 723 pages covers in a comprehensive and unusually clean-cut way the subject of injuries to the bones and joints. It is divided into six parts. In Part I the repair of fractures, delayed and nonunion, adhesions and joint stiffness, soft tissue, vascular and nerve injuries complicating fractures, clinical and radiologic diagnosis, the reduction and immobilization of fractures, and open and infected fractures are discussed. This section is perhaps the most outstanding in the book and abounds in facts and information of fundamental importance. Pathologic and birth fractures comprise Part II. Injuries of the head and trunk, with special emphasis on fractures of the spine and head, are discussed in Part III. This section of the book is also outstanding by reason of the lucid manner in which the material it contains is presented. Part IV takes up injuries of the upper limb, and Part V, injuries of the lower limb. While the material in these sections is excellently presented, they contain little that is new; unfortunately, internal fixation as a method of treatment in fractures of the extremities is largely ignored. The discussion of new and unusual cases in Part VI is interesting but does not add greatly to the value of the book. The appendix, which offers a plan of organization of a fracture service, contains some very valuable suggestions

and is worthy of careful study by those interested in organized fracture treatment. The index of authors and a general index provide a comprehensive bibliography of present-day fracture treatment.

Throughout the book, adequate immobilization of fractures, the necessity of avoiding unnecessarily immobilizing adjacent joints, the importance of active use in restoring function, and the ineffectiveness and harm of passive motion are constantly emphasized. The soundness of the views expressed cannot be questioned, and the precepts laid down are worthy of wide dissemination among those interested in fracture treatment.

The subject matter throughout is presented in a clear, concise manner and leaves no doubt in the mind of the reader as to what the author intended to express. This is true to an unusual degree. The illustrations and the x-ray reproductions are excellent and numerous and illustrate the text splendidly.

As a treatise on the nonoperative management of fractures and joint injuries, this book is important in a day when nearly every book on fracture treatment deals so largely with open reduction and the use of internal fixation. It is for this reason as well as the soundness of the principles it emphasizes that this book can be highly recommended as an excellent addition to the library of anyone interested in fracture treatment.

Die Chirurgie des praktischen Arztes unter besonderer Berücksichtigung der kleinen Chirurgie und der dringlichen Chirurgie. By Erich Sonntag. Ed. 2. Pp. 1,016, with 780 illustrations. Leipzig, 1939, Georg Thieme. 46 marks.

This is a textbook of general surgery written primarily for the students and practicing physicians of Germany. The book is divided in two parts, the first of which, comprising almost one-half of the text, is concerned with surgical principles and fundamentals, such as asepsis, anesthesia, hemorrhage, infections, and wound healing. The second half is devoted to surgical affections of various organs and is arranged in classical regional style beginning with the head and ending with the feet. About thirty pages at the end of the book are devoted to various drugs used in surgery.

The minor surgical procedures are well presented, but the author has made little attempt to include many recent advances in major surgical affections. Thus, for example, decompression by suction applied to an inlying duodenal tube is not even mentioned in the treatment of intestinal obstruction. In the discussion of parasitic diseases the author's statement regarding the transmission of *Taenia solium* is not in accordance with accepted facts. In the chapter on diseases of the liver the important subject of amoebic abscess is merely mentioned. However, the book may be readily recommended to the student as a manual of minor surgery. It is concisely written and the numerous illustrations are well reproduced.

Synopsis of Obstetrics. By Jennings C. Litzenberg, M.D., F.A.C.S. Pp. 376, with 157 illustrations, with 5 in color. St. Louis, 1940, The C. V. Mosby Co. \$4.50.

This excellent little volume of 376 pages and 157 illustrations, including 5 in color, is heartily recommended as an introduction to obstetrics.

The organization of the material is extremely good and is presented in a very clear, concise, and intelligent manner. Despite the fact that the volume is a synopsis, a large amount of valuable material is included which cannot be found in larger and more voluminous textbooks.

Throughout this volume, the author's well-founded conservatism is reflected. The illustrations are good and materially enhance the value of this volume.

Frank Howard Lahey Birthday Volume, June 1, 1940. By many authors. Cloth. Pp. 466, with 68 illustrations. Springfield, Ill., 1940. Charles C. Thomas, Publisher.

On the anniversary of his sixtieth birthday, a number of friends and colleagues contributed this collection of essays, about fifty in number, to do honor to one of America's versatile surgeons who has become widely known. The essays embrace a wide variety of subjects. The majority of the papers, however, concern well-known interests of Dr. Lahey; namely, surgical aspects of diseases of the stomach and duodenum, colon, biliary tract, and the thyroid gland.

Two of the papers are of unusual interest. One of these, under the authorship of Aaron and Murphy, of Buffalo, describes the gastrosopic reappearance of a normal gastric mucosa in patients having pernicious anemia and an atrophic gastric mucosa, following treatment with liver extract. The other, a paper written by Ivy, of Chicago, under the title of "Gastro-Intestinal Hormones," describes very briefly a new hormone which Ivy designates as urogastrone, a substance recovered from male and female urine, which on intravenous injection inhibits the gastric secretory response to histamine.

Ten papers in the volume concern themselves with varying aspects of the ulcer problem. The divergence of views expressed in these papers is striking and suggests how unsettled the problem is.

A Textbook of Bacteriology. By Hans Zinsser, M.D., and Stanhope Bayne-Jones, M.D. Ed. 8. Cloth. Pp. 990, with 115 illustrations. New York, 1939, D. Appleton-Century Co. \$8.

Since its first appearance in 1910, this book has gone through eight editions. New developments in bacteriology and immunity have necessitated the inclusion of much new material and the revision of old. In many respects, therefore, this eighth edition is a new book as compared with the seventh edition of 1934.

Intended primarily for undergraduate students of medicine, the book at the same time should have a wide appeal to practitioners of medicine. Much of the subject matter is taken up with the morphology of bacteria, classification, the properties of bacteria and the effect of physical and chemical agents on bacteria. There is much material of a decidedly practical nature in the book, of particular interest to those whose function it is to apply in practice the principles of bacteriology and immunity. The introductory chapter on the history of bacteriology is especially deserving of mention. The book is well written and the subject matter has been subdivided carefully on a well-ordered plan. The collaboration of the two well-known Professors of Bacteriology, Zinsser and Bayne-Jones from the medical schools of Harvard and Yale Universities, has produced an excellent and authoritative text.

Treatment of War Wounds and Fractures, With Special Reference to the Closed Method as Used in the War in Spain. By J. Trueta, M.D. Foreword by H. Winnett Orr, M.D. Cloth. Pp. 148, with 48 illustrations. New York, 1940, Paul B. Hoeber, Inc. \$2.50.

This small monograph presents a summary of the author's experience in the treatment of war wounds in the recent Civil War in Spain. The book contains an excellent historical account of the development of the treatment of open wounds of the extremities by immobilization in casts of plaster of Paris. Special con-

sideration is given the technical details of the management of injuries involving the various bones and joints of each extremity. The book can be recommended as an important contribution to the importance of immobilization in the management of injuries of the extremities.

Artificial Pneumothorax: Its Practical Application in the Treatment of Pulmonary Tuberculosis. Edited by Edward N. Packard, M.D., John N. Hayes, M.D., and Sidney F. Blanchet, M.D. Foreword by E. R. Baldwin, M.D. Cloth. Pp. 300, with 85 illustrations. Philadelphia, 1940, Lea and Febiger. \$4.

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SURGERY

VOL. 8

DECEMBER, 1940

No. 6

Original Communications

Symposium on Carcinoma of the Lung

MORPHOLOGIC ASPECTS OF CARCINOMA OF THE LUNG

BÉLA HALPERT, M.D., NEW ORLEANS, LA.

(From the Departments of Pathology and Bacteriology of Charity Hospital of Louisiana at New Orleans and the Louisiana State University School of Medicine)

MANY recent contributions emphasize the importance of carcinoma of the lung as a clinical problem. From them it is evident that during the past two decades the number of patients with this condition has increased alarmingly, that the clinical methods of recognition have been improved, and that many laudable attempts have been made to alleviate it. The reason for the increased incidence is still unknown. It seems likely, however, that changed environmental conditions, newly acquired habits, and the increase in the number of persons reaching late middle life and old age have something to do both with the cause of the disease and with the increase in its incidence. With the ample opportunities available for the study of carcinoma of the lung at necropsy, more information can be gathered about the relative frequency, the race, sex, and age incidence, the sites of occurrence, the gross appearance, the probable cellular origin, the cellular structure, and the mode of spread of these growths. Such information is perhaps the safest guide to the early recognition and rational treatment of carcinoma of the lung, as it is of carcinomas arising elsewhere.

Relative Frequency.—Recent surveys of malignant neoplasms in the necropsy material of Charity Hospital of Louisiana at New Orleans by Ogden, Pearson, D'Aunoy, and Halpert¹⁻⁴ disclosed the following pertinent data: Among 7,433 necropsies on individuals over 1 year old, which were performed between Jan. 1, 1931, and June 30, 1939, there were 92 cases of carcinoma of the lung, 169 cases of carcinoma of the stomach, 50 cases of carcinoma of the pancreas, and 56 cases of carcinoma of the biliary system. In the Charity Hospital necropsy mate-

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rial, therefore, carcinoma of the lung was more than one-half as frequent as carcinoma of the stomach and almost as frequent as carcinoma of the pancreas and carcinoma of the biliary system together.

Race, Sex, and Age Incidence.—Three thousand one hundred and seventy of the 7,433 necropsies were performed upon white and 4,263 upon colored subjects, a proportion of 3:4. Carcinoma of the lung, however, occurred 53 times among the white and 39 times among the colored subjects. In the total necropsy material there were 4,801 males (2,183 white, 2,618 colored) and 2,632 females (987 white, 1,645 colored), a proportion of almost 2:1. Carcinoma of the lung, however, occurred 86 times among the males (48 white, 38 colored) and six times among the females (5 white, 1 colored). The youngest patient was 21 and the oldest 75 years of age. One died in the third, 4 in the fourth, 16 in the fifth, 39 in the sixth, 27 in the seventh, and 5 in the eighth decade of life. Seventy-seven per cent of the patients with carcinoma of the lung were thus in the sixth decade of life or older.

Sites.—The main growth was located in the right lung in 49 cases and in the left in 38. In the remaining 5 cases the site could not be determined. Carcinoma of the lung thus occurred somewhat more frequently on the right than on the left side. In 42 cases the primary growth was located in the right or the left bronchus, 10 in this group being located at or near the bifurcation of the trachea. Thirty-five growths were located in a branch of a bronchus. In almost one-half of the cases in this series, therefore, the growths were in a situation accessible to bronchoscopic visualization but in many instances, because of their location at or near the bifurcation of the trachea, they were inaccessible to operative removal.

Gross Appearance.—In the 92 cases which comprise this series the diameter of the mass which formed the primary growth varied from 2 to 15 cm. In the early stages, however, the growth may be represented by a nodule in the mucosa only a few millimeters in diameter; this nodule later may grow to a bulky mass 15 cm. or more in diameter and may replace almost an entire lobe of the lung. The bronchus or the branch in which the growth arises is usually somewhat off center of the contiguous tumor mass. The bronchial wall is eccentrically thickened and the mucosal surface is usually somewhat ulcerated about the area of maximum involvement. Narrowing of the lumen, with obstruction, is more frequently caused by infiltration than by projection of the growth into the lumen.

The gross appearance of the neoplasm depends less on the actual cellular structure of the growth and its stroma than on the size, the extent of involvement, and, in particular, the amount of softening, necrosis, hemorrhage, and secondary changes in the involved and adjacent pulmonic tissue. The gross appearance, therefore, yields no defi-

nite criteria by which the microscopic structure of the carcinoma can be predicted with any degree of certainty. The malignant character of the growth is usually evidenced by the excess of gray or yellow-white tissue of varying consistency, which is dotted with red and brown areas of discoloration and with opaque areas of necrosis or softening. The blotting out of the pulmonary tissue by the neoplasm, the borders of which are indefinite, and the thickening and ulceration of the tributary bronchus or its branch, usually with involvement of the pleura and of one or more of the lymph nodes in the hilus, complete the picture of carcinoma of the lung progressing to the advanced stage.

Cellular Origin.—The concept that the parent cell of all carcinomas of the lung is the reserve cell has been set forth elsewhere.⁵ Some of the reserve cells, like the basal cells of the epidermis, are lined up along the tunica propria, and their oval or elongated nuclei form one or several rows. Their cytoplasm is scanty and their cell borders are scarcely discernible. The ciliated columnar cells and the goblet cells are ordinarily replenished from them. The reserve cells appear to be the only epithelial cells in the mucous membrane of the bronchial tree which are concerned with cell division and cell differentiation. They naturally possess, also, the qualities of their ancestor cells in that they may differentiate into any kind of epithelium which an endodermal cell is capable of producing. If we assume with Whitmore,⁶ then, that the epithelial cells which replace other epithelial cells in a given area retain their embryonic potentialities, it is easy to see how in the course of forced and frequent cell division dominant characteristics may be supplanted by recessive ones, and how stratified squamous epithelium may be produced by the reserve cells. Such a concept offers a logical explanation for the variety in the cellular structure of carcinoma of the lung.

Cellular Structure.—On the basis of the individual and group characteristics of the neoplastic cells, carcinomas of the lung are classified as squamous-cell, columnar-cell, and reserve-cell carcinomas.

The growths are classified as squamous cell when the tumor cells are arranged more or less concentrically to form epithelial pearls, and the cells toward the centers of the cell nests disclose varying degrees of keratinization or are transformed into keratinized scales or debris (Figs. 1 and 2). The coincident presence of columnar cells which form acinar or tubular structures and of undifferentiated or reserve cells alone or in combination does not alter the grouping.

The growths are classified as columnar-cell carcinomas when the tumor cells are columnar or cuboidal and are arranged in acinar, tubular, or papillary structures (Figs. 3 and 4). The presence of additional masses of undifferentiated or reserve cells does not alter the grouping.

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The growths are classified as reserve-cell carcinomas when the tumor cells are of the same size; their nuclei are round, oval, or elongated and stain deeply; their cytoplasm is scanty, and their borders are scarcely discernible (Figs. 5 and 6). The cellular arrangement forms no particular pattern; in some growths the cells are arranged in whorls, in others there is a palisade arrangement of the peripheral cells.

Among the 92 cases of carcinoma of the lung which were analyzed, 49, over 50 per cent, were squamous cell; 17, approximately 20 per cent, were columnar cell; and 26, approximately 30 per cent, were reserve-cell carcinomas. In each of the three types there was considerable variation in the rapidity of growth, the amount and character of the stroma, the degree of inflammatory reaction in the stroma, and the extent of such secondary changes as hemorrhage and necrosis.

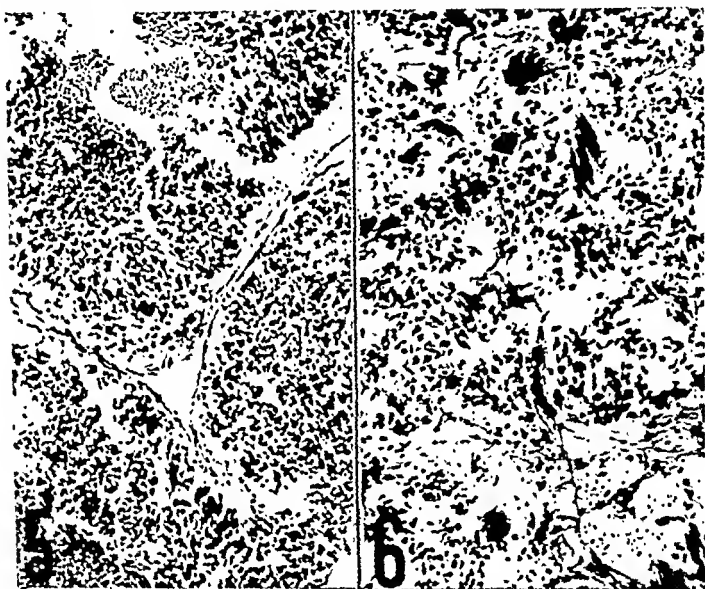


Fig. 5.—Reserve-cell carcinoma of the lung (59-year-old white male). The tumor cells are of about the same size; their nuclei are round, oval, or elongated, and stain deeply. The cytoplasm is scanty and the cell borders hardly discernible. Areas of necrosis are extensive in the centers of the cell nests (Autopsy No. 36-204).

Fig. 6.—Reserve-cell carcinoma of the lung (57-year-old white male). The tumor cells are of about the same size and are arranged in no particular pattern. The connective tissue stroma is scanty and delicate (Autopsy No. 31-99).

Manner of Spread.—The growth usually originates in the mucous membrane of a bronchus or one of its branches and extends into the deeper layers, involving the underlying pulmonic tissue. There is usually also a lateral extension in the mucous membrane which causes unevenness of the surface, eventually followed by ulceration. Local extension by contiguous growth and through the lymph and blood channels usually causes involvement first of the regional lymph nodes, then of the pleura, and later of more distant groups of lymph nodes, as well as metastases into distant organs.

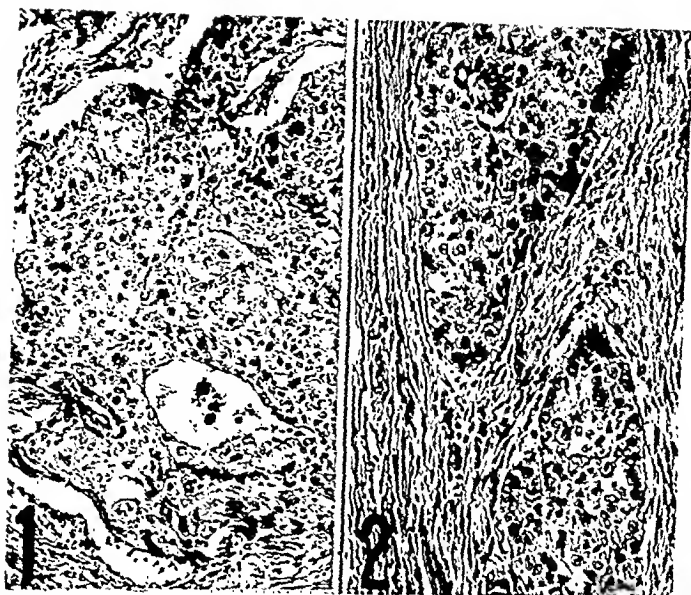


Fig. 1.—Squamous-cell carcinoma of the lung (59-year-old colored male). The cells toward the center of the cell nests disclose varying degrees of keratinization (Autopsy No. 38-114).

Fig. 2.—Squamous-cell carcinoma of the lung (56-year-old colored male). The cells toward the center of the cell nests disclose varying degrees of keratinization and a cellular debris (Autopsy No. 39-2).

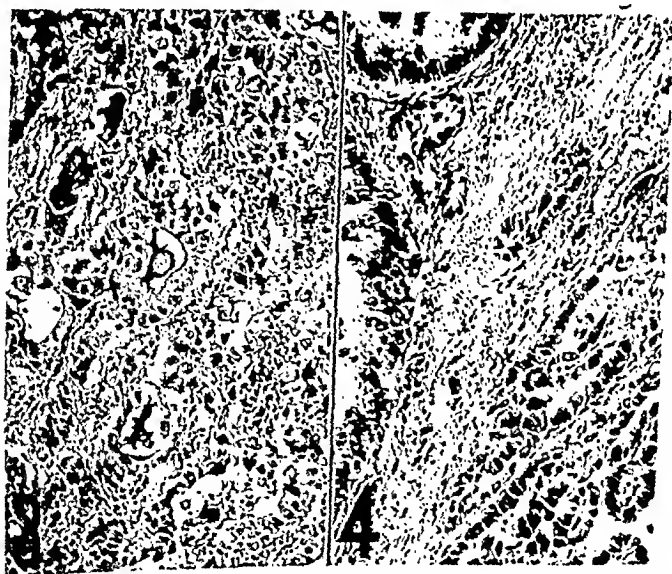


Fig. 3.—Columnar-cell carcinoma of the lung (49-year-old white male). The columnar or cuboidal cells in acinar or tubular arrangement simulate in a haphazard way normal epithelial structures of the air passages. The lumina of the acinar or tubular structures contain a pink or lavender staining secretion (Autopsy No. 36-346).

Fig. 4.—Columnar-cell carcinoma of the lung (51-year-old white female). The columnar cells are mounted on connective tissue stalks in a papillary arrangement (Autopsy No. 34-597).

somewhat more frequently on the right side than on the left. In almost one-half of the cases the primary growth was located in the right or the left bronchus. The gross appearance yielded no definite criteria by which the microscopic structure of the carcinomas could be predicted with any degree of certainty. Over 50 per cent of the growths in this series were squamous-cell, about 20 per cent columnar-cell, and about 30 per cent reserve-cell carcinomas.

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Local extension with involvement of the regional lymph nodes occurred in 81 of the 92 cases. Extensive distant metastases occurred in 53 cases. Metastatic foci were encountered in the liver 28 times, in the suprarenal glands 13 times, in the kidneys 11 times, and in the pancreas and in the skeleton 9 times each.

COMMENT

It should be emphasized that the data just presented concern with few exceptions patients in whom carcinoma of the lung was the principal lesion and the immediate or contributory cause of death. In such cases the lesions are naturally far advanced, yet an analysis of the material offers much of interest.

Males between the ages of 41 and 60 years apparently comprise the majority of patients with carcinoma of the lung. The site of origin may be in either lung, and is usually in a bronchus or in one of its branches. In those instances in which the growth is easily seen through a bronchoscope, the operability is frequently poor because of the proximity of the growth to the bifurcation of the trachea. More amenable to surgical treatment, although less easily accessible to bronchoscopy, are those growths which arise in a branch of the bronchus.

Radiation therapy in carcinoma of the lung, as in carcinoma in other locations, depends upon the radiosensitivity of the neoplasm and its accessibility to adequate radiation. The cellular structure and the frequency with which the three types of carcinoma occur in the lung (over 50 per cent squamous-cell, about 20 per cent columnar-cell, and about 30 per cent reserve-cell) give the radiotherapist clues as to the result to be expected from radiation therapy.

The story remains to be told of a series of cases in which early recognition has led to prompt removal of the lung containing the growth.⁷ A collection of such cases will soon be available for histologic analysis, and it will be of great interest to ascertain whether or not a particular type of carcinoma of the lung lends itself to early detection and to the application of successful therapeutic measures.

SUMMARY

Among 7,433 necropsies on individuals over 1 year old there were 92 carcinomas of the lung, more than one-half as many as carcinomas of the stomach and nearly as many as carcinomas of the pancreas and the biliary system together. Seventy-seven per cent of the patients with carcinoma of the lung were in the sixth decade of life or older. The proportion of whites to negroes in the total number of necropsies was approximately 3:4; whereas, carcinoma of the lung occurred in the proportion of about 1.4:1. The proportion of males and females in the total number of necropsies was almost 2:1; whereas, carcinoma of the lung occurred in the proportion of about 14:1. The growth occurred

These four statistical studies are similar in that the largest percentages fall in the fourth, fifth, and sixth decades. However, there are a sufficient number of cases in the younger-age group to warrant serious consideration of the presence of malignancy when the clinical signs and symptoms are suspicious.

Schwytzer⁵ reported an adenocarcinoma of the lung in a 16-month-old child. The patient became ill two months before her death, with loss of appetite and pallor. The left half of the thorax was entirely obscured by an effusion and there was extreme dyspnea. Death was due to diphtheria, and at autopsy the left lung was found to be invaded by a large mucoid tumor which extended diffusely through the parenchyma, leaving only a little atelectatic pulmonary tissue posteriorly.

Sex.—The question of sex in relation to carcinoma has also been studied by numerous authors. In my own series² of 56 cases, 42 were males, and 14 females. In Fried's¹ series of 152 cases, 123 were males and 29 females. Fereney and Matolesy,⁶ of Vienna, reported 282 cases, 204 of whom were males and 78 females. In the series reported by Frisell and Knox⁴ of 46 cases, 36 were males and 10 females. A total of these statistics show 536 cases, of which 405 are males and 131 are females.

The predominance of carcinoma of the lung in males may be due to the fact that they are more susceptible to pulmonary irritation than are women and also that women develop carcinoma of the generative organs in a greater degree than men and die of this condition early in life. At present we are unable to state just why the proportion of male to female is so high.

Location of Tumor.—Fried¹ collected 1,639 cases from the literature; 1,034, or 63.7 per cent, occurred on the right side and 605, or 36.1 per cent, on the left. Bieberfeld² found 154 carcinomas in the right lung and 53 in the left, and Seyfarth² reported 258 right-sided cancers and only 49 left-sided. Fischer⁷ reports in a series of 3,735 cases that 53 per cent occur on the right and 45 per cent on the left.

The location of the tumor in the right lung is more frequent than in the left, but, when one finds any lesion in the right or left lung, that fact does not lend much weight when considering the possibility of carcinoma because of the location.

Symptoms.—The early subjective symptoms of carcinoma of the lung vary so widely in different patients that it is difficult to decide when a patient's complaint may indicate the beginning of a malignant disease of the lung. Undoubtedly microscopic cells occur in the bronchus before symptoms appear and it is not until they involve structures which might produce pressure, pain, or hemoptysis that an individual will seek medical help. There have been attempts to classify the first symptoms in some series of cases.

PRIMARY BRONCHIOGENIC CARCINOMA

A CLINICAL STUDY

J. J. SINGER, M.D., LOS ANGELES, CALIF.

(From the Rose Lampert Graff Foundation and the Cedars of Lebanon Hospital)

THOROUGH and exhaustive clinical studies of carcinoma of the lung have been undertaken with the expectancy that there would emerge definite clinical patterns, each pattern capable of recognition and representing a certain underlying pathologic process.

It is evident from the numerous reports thus far presented on this subject that a definite diagnosis of bronchiogenic cancer cannot be made without biopsy specimen and microscopic studies. However, we have learned a great deal from these studies, particularly a proper evaluation of important symptoms and signs as well as methods of differentiation from other pulmonary diseases.

In order to discuss this subject in detail, I will consider the following: age, sex, location of lesion, first symptoms, complications (such as bronchitis, emphysema, atelectasis, abscess, bronchiectasis, tuberculosis, silicosis, and infection), occupation, duration of disease, and methods of diagnosis in relation to bronchiogenic carcinoma, and analyze each separately.

Age.—The age incidence of carcinoma of the lung is approximately the same as for cancers of all other organs. The majority of cases occur between the fortieth and seventieth years, and rarely below the age of 20 years. Statistical studies have been made by Fried¹ at the Montefiore Hospital (New York); Graham, Singer, and Ballou² at Barnes Hospital (St. Louis); Maxwell and Nicholson³ from Brompton Hospital (London); and Frissell and Knox⁴ from St. Luke's Hospital (New York), as well as by others.

TABLE I
AGE INCIDENCE OF BRONCHIOGENIC CARCINOMA

| AGE YEARS | NO. OF CASES | | | | TOTAL |
|--------------|------------------------|--------------------|----------------------|------------------------|-------|
| | MONTEFIORE HOSPITAL | BARNES HOSPITAL | BROMPTON HOSPITAL | ST. LUKE'S HOSPITAL | |
| Under 30 | | 1 | 8 | 4 | 13 |
| 30-40 | 11 | 6 | 20 | 5 | 42 |
| 40-50 | 27 | 13 | 41 | 6 | 87 |
| 50-60 | 52 | 23 | 30 | 17 | 122 |
| 60-70 | 45 | 10 | 5 | 14 | 74 |
| 70-80 | 15 | 3 | 3 | | 21 |
| 80-90 | 2 | | | | 2 |
| Total | 152 | 56 | 107 | 46 | 361 |

These four statistical studies are similar in that the largest percentages fall in the fourth, fifth, and sixth decades. However, there are a sufficient number of cases in the younger-age group to warrant serious consideration of the presence of malignancy when the clinical signs and symptoms are suspicious.

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Carlson and Ballou⁸ analyzed the symptoms of 26 cases (autopsied) at the Barnes Hospital, St. Louis. They classified the symptoms of these cases into three groups: (1) local pulmonary symptoms, (2) general symptoms, and (3) symptoms suggestive of extension or metastasis. Table II shows the number of complaints according to frequency in these cases.

TABLE II*
SYMPTOMS UPON ADMISSION TO HOSPITAL (26 NECROPSY CASES)

| | NO. OF CASES |
|--|--------------|
| <i>I. Local pulmonary symptoms (grouped according to frequency)</i> | |
| Cough | 17 |
| Chest pain or discomfort | 11 |
| Dyspnea | 11 |
| Sputum | 10 |
| Hemoptysis or "streaking" | 6 |
| "Chest colds" | 2 |
| (No chest symptoms 5) | |
| <i>II. General symptoms</i> | |
| Weight loss | 9 |
| Weakness | 6 |
| Anorexia | 3 |
| Night sweats | 2 |
| Thirst | 1 |
| Fatigue | 1 |
| <i>III. Symptoms suggestive of "extension," metastases, or unrelated disease</i> | |
| Nervous symptoms | 8 |
| Pain in back or extremities (not related to nerve pathways) | 7 |
| Urinary symptoms | 3 |
| Vomiting | 2 |
| Abdominal pain | 2 |
| Abdominal enlargement | 1 |
| Engorgement of veins | 1 |
| Precordial distress | 1 |
| Dysphagia | 1 |

*Patients observed at the medical and surgical chest service, Barnes Hospital, St. Louis.

The cough is usually dry, harassing, and occasionally accompanied by blood-streaked sputum, and rarely frank hemoptysis. Chest pains are most significant and seem to be, especially in the early cases, much more severe than the physical signs would warrant; but in the absence of definite pleurisy and in the right age groups one must consider pain as an important symptom of the disease under discussion.

Dyspnea, which may become the most distressing symptom of all, does not occur early unless sudden atelectasis has taken place. In the slow contraction of the lung, dyspnea does not occur so readily, even when an entire lung is involved.

Weight loss does not occur early in the disease. The reason for this may be that this symptom develops when there is secondary involvement of other organs. Cachexia does not manifest itself until very late in the disease. Night sweats, fever, Horner's syndrome and clubbing of nails are also late symptoms.

The signs of metastasis are too varied for classification, but, when patients have signs of involvement of the lung and develop signs of metastasis to other organs, it must be considered as part of the same process.

The blood picture is not significant.

Because of recent therapeutic advance, particularly surgical approach, carcinoma of the lung can no longer be considered a hopeless condition. Consequently the clinical discovery of early cases becomes imperative.

Duration.—The duration of the illness, before the patient is aware of any involvement of his lung, varies from a few days to as long as twenty years. Some patients are more observing than others and, strangely enough, a rather large percentage of patients do not come until late in the disease and not then unless there is hemoptysis or excruciating thoracic pain. A careful history, however, of patients who might be suspected of having the disease will reveal conditions to the patient himself which may be significant in the true interpretation of the cause of the symptoms. Most of the patients, however, manifest the important symptoms which precede their death from one to fifteen months.

Occupation.—The occupation of patients who have carcinoma becomes important, particularly when carcinoma apparently follows some traumatic injury; especially for those persons who work where there is a hazard of trauma, particularly in coal mines, in an atmosphere of silica dust, or where inhalation of tar fumes is likely. In the well-known mining district of Schneeberg many cases of carcinoma have developed in the workers. There many investigators attribute the carcinoma to the inhalation of arsenic and cobalt, while others feel that it may be due to the inhalation of silica dust.

Lynch and Smith⁹ report a case of carcinoma of the lung due to asbestosilicosis. This man was 57 years of age when he was first examined. His chief complaints were pain in the right side of the stomach and right side of the back and shoulder and shortness of breath. He had been exposed to dusty atmosphere when 16 years of age, working as a weaver in a cotton mill. Twenty years later he began to work as a weaver in an asbestos factory, a position he held up to the time of his entry into the dispensary in 1934. A diagnosis of silicosis and asbestosis was made and at autopsy an associated carcinoma was found in the lower lobe of the left lung. These authors feel that the chronic bronchial irritation was compatible with the current etiology of the carcinoma. In other words, they believe that the irritation of the bronchi may be a hazard of the type of work done in the development of carcinoma. However, it is so rare that one finds carcinoma associated with either silicosis or asbestosis that one may assume that the disease occurs in a patient who has other pulmonary involvement.

In a case I saw at the Barnes Hospital, St. Louis, a miner was struck by a small truck which pinioned him against the wall of the mine. He

developed bleeding from the lung which lasted for over a year. He died later and at the post-mortem examination a carcinoma was found in the lung in addition to the silicosis.

Experimental production of carcinoma by the exposure of mice to coal-tar fumes and also to exhaust from automobiles and by the painting of mice with tar apparently has no correlation to the development of carcinoma of the lung in man.

There are a great many workers in all occupations who develop carcinoma, though they are in no known way exposed to occupational hazards. This leaves the problem of the relationship of carcinoma to occupation still a question for study.

Types of Carcinoma of the Lung.—It is accepted by nearly all workers that carcinoma of the lung arises from the bronchial mucosa and not from the alveolar epithelium. Fried¹ has shown conclusively and it has been proved by others that the alveoli do not contain fixed cells which can produce carcinoma. He states:

“Carcinoma originating primarily in the lungs is bronchiogenic.

“There is evidence that when the disease is found in the lungs it results from a pathologic (excessive) regeneration following chronic inflammation of the bronchial tree.

“Of the three varieties of cells lining the bronchial mucosa, that is, the ciliated columnar epithelium, the goblet cells and the ‘basal’ cells, only the last are concerned in the process of regeneration of the bronchial mucous membrane. It is assumed, therefore, that these cells likewise serve as a sole matrix for primary bronchiogenic tumors.

“Similarly, primary squamous cell epitheliomas and basal cell epitheliomas of the lungs do not result from metaplasia of the pre-existing ciliated columnar epithelium, but originate through protoplasia (indirect metaplasia) of the undifferentiated basal cell of the bronchial mucous membrane.”

Grossly, the types of carcinoma, as shown by the roentgen-ray film, have been classified by Lenk¹⁰ as follows: (a) pure intrabronchial tumors, (b) carcinomatous pneumonia, (c) hilus carcinomas, (d) carcinoma involving a lobe, (e) the so-called lymphangitis carcinomatosa, and (f) interlobar carcinomatous nodules.

It must be appreciated that a roentgen-ray picture is due to not only the tumor mass but also the effects upon the bronchial tree; that is, atelectasis, bronchiectasis, or pneumonia. The roentgen-ray appearance may be due to metastases, a pleural effusion, pleural thickening, abscess of the lung, gangrene, or obstructive emphysema. There may be much fibrosis, pleural thickening and distortion of the mediastinum so that the picture is one of the unilateral opacity of the type which suggests a chronic fibroid tuberculosis.

In view of such different structures, therefore, the variations of symptoms and physical signs accompanying such changes must be expected.

Complications of Bronchiogenic Carcinoma.—Among the most important complications are: atelectasis of the lobe or lobes or even the entire lung, abscess, bronchiectasis, empyema, emphysema, bronchitis, and spontaneous pneumothorax.

Atelectasis is a condition which is produced by the presence of an intrabronchial mass which may block a main bronchus or one of the smaller bronchi, depending on where the tumor originates. The usual signs of massive atelectasis may be found sometime in the early papillomatous type so that one must not consider a complete density in a roentgen-ray film as evidence that the carcinoma itself is as extensive as the shadow would indicate. It is well known that, when bronchi are obstructed and atelectasis develops, infection of the pulmonary tree distal to the obstruction is frequently the site of abscess formation produced by anaerobic bacilli. Secondary to these abscesses it is not uncommon for bronchiectasis to develop. This triad of complications is most frequently met with in the majority of carcinoma of the lung, but it requires considerable diagnostic ability to be able to unravel the complications from the disease itself. Fortunately, with our present means, which will be discussed later, this so-called mystery of the shadows can be solved.

Accompanying diseases, such as tuberculosis, silicosis, and emphysema, do not seem to be complications as much as separate diseases in the same patient. A rather important complication is the development of fluid in the chest as a secondary manifestation of irritation. The original pulmonary involvement may be the lymphangitis carcinomatosa and this condition is rarely diagnosed except when there are metastatic lymph nodes available for biopsy or at a post-mortem examination, and then only when microscopic sections of the lung are studied.

Diagnosis.—The clinical diagnosis of carcinoma of the lung must be confirmed by many tests, but the only positive one is the finding of carcinoma cells in the lung tissue. The correct diagnosis in the past five years of this condition has risen from approximately 20 per cent to between 75 and 90 per cent of cases. This marked advance in more correct diagnosis has followed the more careful and exhaustive studies developed in the chest centers.

Physical Signs.—The signs elicited in a suspected case of carcinoma of the lung depend on the size, shape, and location of the tumor. In the miliary type no definite signs are noted, but, when the mass is large, dullness, bronchovesicular breath sounds, and increased whisper sounds are present. Râles may or may not be heard. Areas of emphysema may so surround the smaller masses that the signs of a mass are not elicited. In a patient who was under my care, the signs of obstructive emphysema were the only significant change from the normal. In this patient, his advanced age and the history of wheezing, cachexia, and frequent hemoptysis suggested carcinoma. By bronchoscopic examination one

could see the mass partially obstructing the lower right bronchus. Air was able to enter the lobe but could not be forced out on expiration. A microscopic section of a biopsy specimen showed this mass to be a squamous-cell carcinoma.

The physical signs by themselves rarely are of diagnostic value without the other evidences of tumor.

Direct vision, by means of bronchoscopy, enables one to obtain exact information as to what is present in the larger bronchi. Today in all large medical centers well-trained bronchoscopists are available so that mistaken diagnosis by omission of bronchoscopy should not be excused. Removal of bits of tissue can be easily done and microscopic examination of them makes definite diagnosis possible. When the tumor is in the smaller bronchi, the bronchoscopic examination fails. If fluid is present in the pleural cavity, this can be aspirated and air injected. It is now possible to introduce a cannula into the pleural space under local anesthesia. A thoracoscope can be inserted into the cannula and a good view of the entire chest cavity can be obtained. At the same time it is also possible to take biopsy specimens of the pleura or lung tissue.

I have designed a thoracoscope¹¹ which has a universal adapter placed on the proximal end of a small oval-shaped cannula. Two openings in this adapter permit the introduction into the chest cavity of a small thoracoscope of the foreoblique type and operative instruments, such as galvanocautery, high-frequency electrode, long hypodermic needle, biopsy forceps, or catheter. The use of any one of the instruments permits direct vision. If the operator wishes to use the two-cannula method, another puncture is made with a second flat trochar and cannula, and the foreoblique lens is put in one instrument and the various operative instruments are introduced through the second opening. It is obvious then that this universal thoracoscope combines the value of both types of operation and permits the use of either method. Fig. 1 shows how the instrument is assembled.

The pleural fluid can be studied by the Mandelbaum method, which consists of centrifugalizing the fluid and then fixing the sediment as if it were tissue. Microscopic studies are then made. Finally, biopsy specimens may be taken by puncture with a large needle plunged into the mass, or even thoracotomy is indicated at times. Occasionally, even then, the pathologist may report atelectatic lung and fibrous tissue.

Roentgen Ray.—The use of the fluoroscope has been of particular value in our studies. One must spend considerable time in the darkroom before beginning to see the picture on the screen. The faint shadow becomes distinct when the eyes are accommodated and the normal is early distinguished from the abnormal. By fluoroscopy one can visualize patients from many angles and it is not infrequent that a homogeneous shadow in the film "dissolves" in such a way that one can note brilliant lung tissue behind or in front of the mass producing the shadows. The

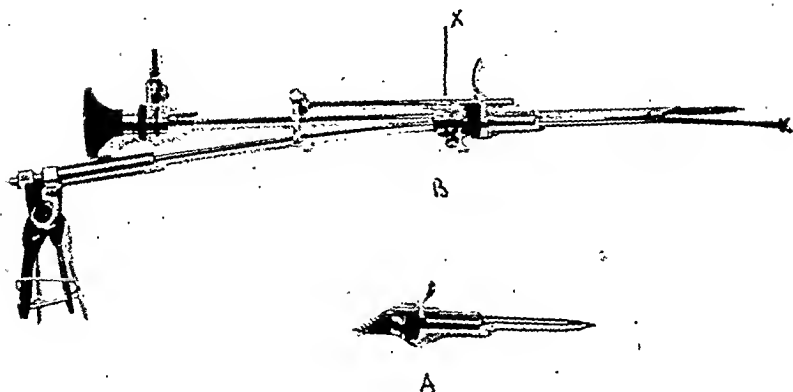


Fig. 1.—Photograph of Singer's universal thoracoscope assembled (made by Phillips-Drucker, St. Louis, Mo.). A shows small oval trochar and cannula; B shows the assembled instrument; X is the universal adapter through which the thoracoscope and operative instruments can be inserted.

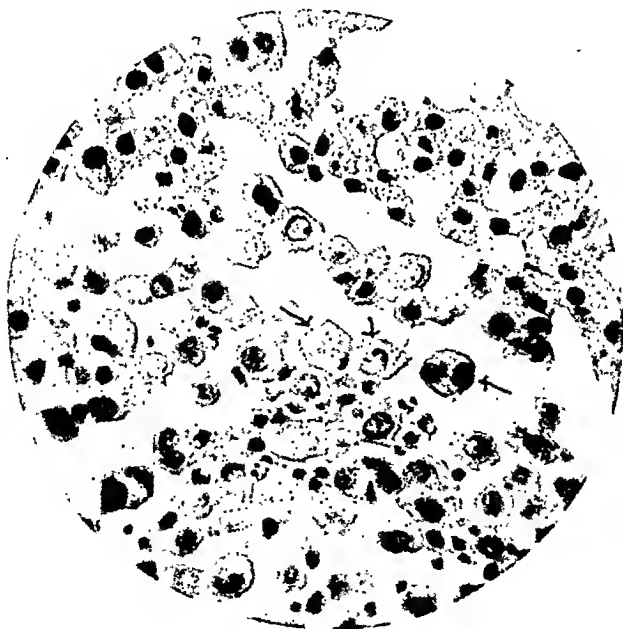


Fig. 2.—Specimen of chest fluid, April 25, 1939. Arrows point to tumor cells. Microscopic examination of paraffin section of centrifuged sediment of 30 c.c. of straw-colored fluid shows a large number of cellular elements; practically no red blood cells are seen. Groups of leucocytes are scattered along larger numbers of tumor cells. These cells vary considerably in shape and size; frequently they are polyhedral to oval; cell borders are distinct or, at times, fused. Cytoplasm is pale and coarsely granular; nuclei are large with, in many instances, large nucleoli. Some of the nuclei have vacuolization probably due to glycogen, but mostly they are light blue; some are hyperchromatic. An occasional bizarre mitotic figure is seen. Some multi-nucleated cells are present. *Diagnosis:* Carcinomatous extension or metastasis to pleura. (X500.)

combination of the physical signs, fluoroscopic examination, and roentgen films affords the factors upon which judgment can be based as to the character of the shadow.

When fluid produces the shadow, it is impossible to visualize the lung; but, when the fluid is aspirated and air is introduced (diagnostic pneumothorax), then roentgen ray becomes of greater value.

It is not unusual to see shadows in the lung which cannot be diagnosed as tumor, but careful study of the roentgen-ray appearance of ribs may show areas of rarefactions and even of spontaneous fractures. Thus, as these may be interpreted as evidence of metastasis in the bones, the shadow in the lung may also be so interpreted.

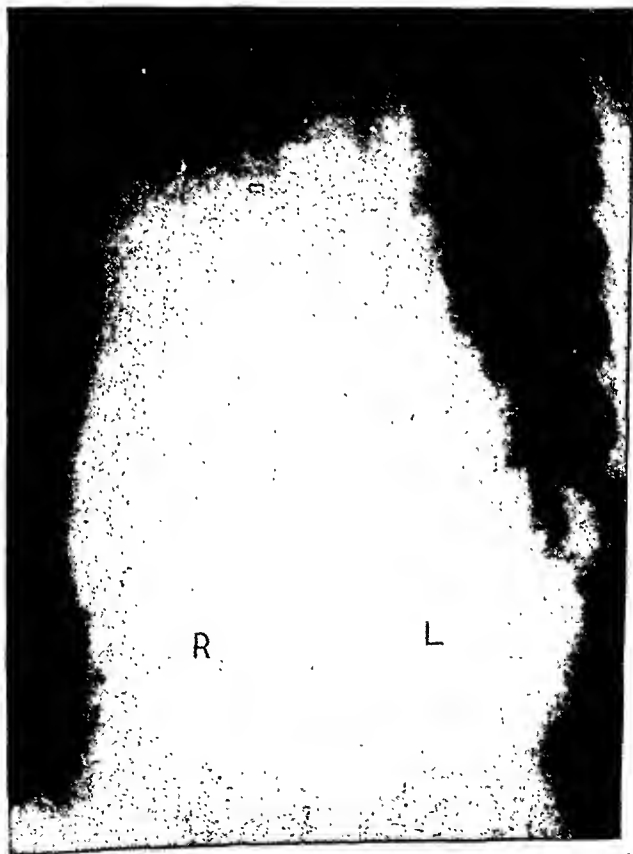


Fig. 3.*—Roentgen film of patient; upright position shows unilateral density on the right chest, except above the second rib. No displacement of mediastinum to the right.

Bronchography, by the use of iodized oil, has added exactness to our diagnostic methods. The closed bronchus and deformed distribution of the bronchial tree are easily recognizable.

*Figs. 3-6 show how one can, by diagnostic pneumothorax, separate the various components which produced the homogeneous shadow in the right chest. Biopsy by thoracotomy proved this mass to be a bronchogenic carcinoma.

The newer methods of taking films by planography or tomography are also of great value in the localization of masses and cavitation.

The details of roentgen-ray studies will be discussed in full by others in this symposium.

CASE HISTORIES

CASE 1.—H. K., white, male, clothes cutter, aged 52 years. Entered Cedars of Lebanon Hospital on April 24, 1939.

His previous history shows that at the age of 32 years, during an attack of a so-called chest cold, he was told by his physician that he had a leaking heart. He did not recall any rheumatic fever and was asymptomatic until six years ago, when he first noticed dyspnea on exertion. Three years later he was forced to sleep

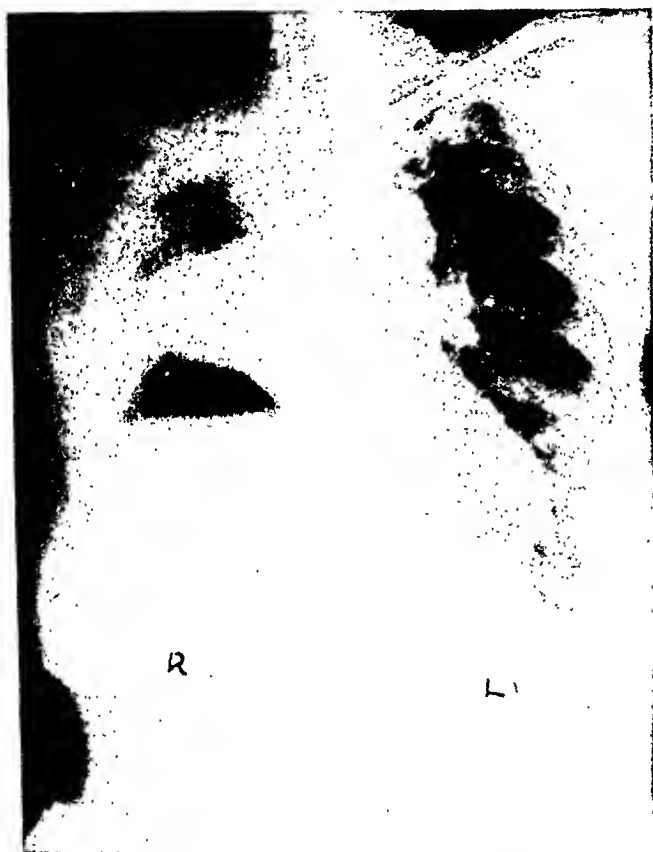


Fig. 4.—Roentgen film of patient, upright position after 500 c.c. of fluid was removed and 200 c.c. of air injected. Note the density between the aerated lung above and the air pocket below. Mediastinum still not shifted.

in a chair because of "asthma." He has had occasional hemoptyses of brief duration in past eight years, and a few attacks of angina pectoris for the past year. He worked until three weeks before he entered the hospital, despite marked ankle edema, dyspnea, and orthopnea.

He entered another hospital at that time and was treated for cardiac decompensation by digitalis, rest, and the aspiration of two quarts of clear fluid from the chest. He did not improve, however. He had pains in the right chest and stated he lost ten pounds in the last year.

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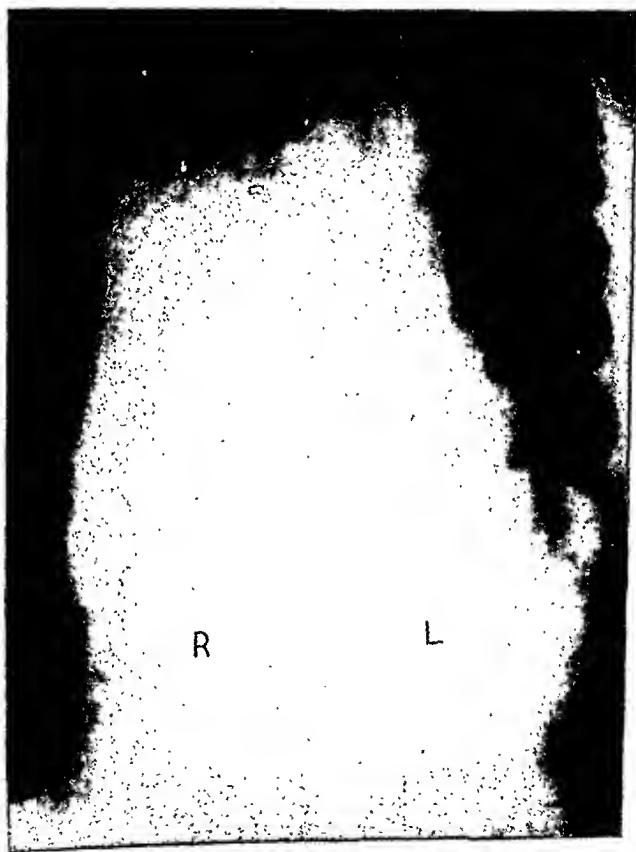


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*Figs. 3-6 show how one can, by diagnostic pneumothorax, separate the various components which produced the homogeneous shadow in the right chest. Biopsy by thoracotomy proved this mass to be a bronchiogenic carcinoma.

Physical examination showed an orthopneic, dyspneic, cyanotic, cachectic male. He showed signs of a large amount of fluid and air in the right chest with marked shift of mediastinum to the left. Heart sounds were faint and he had a systolic murmur at the apex. He showed ankle edema. His circulation time was as follows: venous pressure, 26.4 cm.; arm to tongue time, 27 seconds; arm to lung time, 11 seconds; and lung to tongue time, 16 seconds. These showed signs of decompensation. Three thousand cubic centimeters of bloody fluid was aspirated from the right chest and centrifugalized and the sediment embedded in paraffin. On three occasions this was done and only the first specimen showed some carcinoma cells.

X-ray examination of the chest showed a partial collapse of the middle and lower lobes on the right side. The upper lobe was only slightly collapsed, probably held by pleural adhesions. The density of the atelectatic middle and lower lobes prevented the visualization of an infiltration in the lung tissue.

Thoracoscopy was done on May 20, 1939, in the right chest. There was a small amount of bloody fluid in the costophrenic sulcus. The lung was visualized. The lower part of right lung, which was hard and almost immovable, was adherent superiorly. Its underlying color was densely white and there seemed to be thickening and infiltration of the parietal pleura. Biopsy specimen was removed from the parietal pleura and sent to the laboratory for examination. Microscopic section showed old fibrin mixed with large cells which varied some in size and shape. Numerous hyperchromatic nuclei were present. No mitotic figures were seen. *Diagnosis:* metastatic carcinoma to pleura.

The patient died two days later. A post-mortem examination showed that the right lung was involved by miliary bronchiogenic carcinoma.

Comments.—The history of this case was not suggestive of carcinoma by any of the clinical diagnostic standards that we have. The x-ray examination was not suggestive of a malignancy. However, the clinical inferences as to the possibility of carcinoma were his age, marked loss of weight, hemoptysis, and bloody fluid in the right chest. While he had an associated cardiac decompensation which overshadowed the symptoms of malignancy, careful analysis of the various conditions present lent some weight to the possibility of malignancy and therefore a biopsy through the thoracoscope was done and a positive diagnosis of malignancy was thus obtained.

CASE 2.—M. K., white, male, aged 62 years, entered Cedars of Lebanon Hospital on Feb. 3, 1937.

He had a past history of pneumonia at the age of 23 years. His chief complaints at admission were pain in the right chest, hemoptysis, loss of weight, weakness, and anorexia.

Physical Signs.—In the lungs there was a generalized impairment of resonance over the right lung field by a mass particularly limited to the upper and middle lobe. Occasional moist râles were heard over this area. Breath sounds diminished over this area. Left lung showed no abnormal signs.

X-ray examination of the chest on Feb. 4, 1937, showed a radiopacity over the entire right upper lobe. The trachea and mediastinal contents were not displaced. A radiopaque patch, the size of a walnut, was present at the right hilus, probably due to extension of the tumor mass in the right upper lobe. The right costophrenic angle was slightly obscured, probably by fluid. The pleura was somewhat thickened.

The patient was bronchoscoped on Feb. 8, 1937. The left main stem bronchus was explored and found to be normal in appearance and unobstructed. The orifices



Fig. 5.—Roentgen film of patient, right horizontal lateral position. Air pocket now along the axillary area and shows no abnormal condition other than hazy right diaphragm. The pocket is limited by mass and adhesions at the second anterior rib.



Fig. 6.—Roentgen film of patient, left horizontal lateral position. Air pocket has shifted toward the mediastinum and limited there. One notes a density with concavity downward.

Physical examination showed an orthopneic, dyspneic, cyanotic, cachectic male. He showed signs of a large amount of fluid and air in the right chest with marked shift of mediastinum to the left. Heart sounds were faint and he had a systolic murmur at the apex. He showed ankle edema. His circulation time was as follows: venous pressure, 26.4 cm.; arm to tongue time, 27 seconds; arm to lung time, 11 seconds; and lung to tongue time, 16 seconds. These showed signs of decompensation. Three thousand cubic centimeters of bloody fluid was aspirated from the right chest and centrifugalized and the sediment embedded in paraffin. On three occasions this was done and only the first specimen showed some carcinoma cells.

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CASE 2.—M. K., white, male, aged 62 years, entered Cedars of Lebanon Hospital on Feb. 3, 1937.

He had a past history of pneumonia at the age of 28 years. His chief complaints at admission were pain in the right chest, hemoptysis, loss of weight, weakness, and anorexia.

Physical Signs.—In the lungs there was a generalized impairment of resonance over the right lung field by a mass particularly limited to the upper and middle lobe. Occasional moist râles were heard over this area. Breath sounds diminished over this area. Left lung showed no abnormal signs.

X-ray examination of the chest on Feb. 4, 1937, showed a radiopacity over the entire right upper lobe. The trachea and mediastinal contents were not displaced. A radiopaque patch, the size of a walnut, was present at the right hilus, probably due to extension of the tumor mass in the right upper lobe. The right costophrenic angle was slightly obscured, probably by fluid. The pleura was somewhat thickened.

The patient was bronchoscoped on Feb. 8, 1937. The left main stem bronchus was explored and found to be normal in appearance and unobstructed. The orifices

were similarly normal. An excellent view was obtained of the right upper lobe bronchus. This region presented no inflammatory or neoplastic changes. The orifice was shrunk with neosynephrine and a sponge inserted into the branch to the right upper lobe. There came away on the sponge a large gelatinous, thick, tenacious mucous plug which may well have obstructed this bronchus. No further positive changes were present.

On Feb. 12 thoracentesis was done, with the puncture site between the third and fourth ribs in the posterior-right side. No fluid was obtained.

Punch biopsy was done into the mass on Feb. 25. A few shreds of tissue were obtained, the microscopic report of which was negative for carcinoma. It was then decided that an open thoracotomy should be done to see if the density was due to an abscess. A portion of the third rib was removed posteriorly and biopsy taken of the pleura and attached lung. This was examined microscopically and the section showed mostly fibrous tissue in which there were areas of round-cell infiltration. This can be interpreted as thickened pleura. There was one small piece of lung tissue in which there was considerable atelectasis and the few remaining alveoli were filled with phagocytic cells and blood pigment. No evidence of neoplasm was seen in any of the sections at hand. The patient became weaker and finally died at his home on Jan. 20, 1938. An autopsy revealed the following: The pleural surface of the right lung showed dense, fibrous thickening. The lung was nodular and subcrepitant in consistency. The main bronchus to the right upper lobe just distal to its bifurcation was almost entirely occluded, except for a minute lumen of about 1 mm., by a firm mass of cellular, grayish-white tissue which appeared to rise from the mucosa and which infiltrated into the adjacent lung substance for a distance of about 3 cm. The branches of this bronchus distal to the point of obstruction were dilated and showed a necrotic reddish-purple surface.

Microscopic examination.—Sections from the main mass of the tumor described grossly showed very extensive necrosis of the tumor about the periphery. There were frequent clusters of viable tumor cells. These were arranged in irregular clusters and strands and solid, cellular cords. In many places large areas of tumor tissue were necrotic, except at the very periphery where there were viable tumor cells. Generally the tumor cells were small and undifferentiated. They formed frequent epithelial pearls in places, although it was not possible to demonstrate intracellular bridges in these areas and it was questionable whether these were active epithelial pearls or areas of beginning necrosis. Their appearance and the fact that the tumor remained so well confined to the lung suggested that these were true squamous epithelial pearls. Adjacent and supporting connective tissue showed very dense hyaline fibrosis.

Comments.—The clinical history, symptoms, and signs all pointed to carcinoma: loss of weight, edema, hemoptysis, cough, severe pain, and x-ray. Yet, at no time, in spite of biopsies being made, even with rib resection, was carcinoma positively diagnosed. This case is described to show how, with all means at our command, the final diagnosis at times is made only at autopsy, although clinical signs may be so definite that the patient can be treated as having carcinoma of the lung.

SUMMARY AND CONCLUSIONS

The clinical picture of carcinoma of the lung is still so varied that no definite pattern has been discovered to fit the many types of pathologic conditions present. However, with close observation of the patients and

taking into consideration the many factors discussed, such as age, location, complications, and sex, and also with the aid of the many diagnostic methods, very few cases of carcinoma of the lung are now overlooked. In view of the fact that surgical approach in early cases of carcinoma of the lung has been proved successful in many instances and with the increased proficiency of the surgeons in this field, it behooves all medical men to search out these early cases if we are to benefit our patients. From the analysis of the various circumstances surrounding this subject which has been discussed, certain highlights are present.

These are that, given a patient in the ages between 40 and 70 years, with symptoms of pulmonary disease with special reference to cough, pain in the thorax, and hemoptysis, the examiner should stress his studies in the search for malignancy of the lung as a probable etiologic condition of the patient's complaints. The advances in our diagnostic ability have been for the most part improvements in roentgen-ray technique, bronchography, bronchoscopy, the study of pleural fluids for malignancy cells, thoracoscopic biopsy, and also punch biopsy.

In vague pulmonary diseases, if all the signs remain indefinite for a diagnosis of carcinoma, one should search for evidences of metastasis in the lymph glands of the neck and axillae and evidences of metastasis should be searched for in the brain, ribs, kidneys, and rarely the skin. In cases that have been operated upon for carcinoma elsewhere, even as long as twenty years before, studies of the chest should be made for metastatic involvement of the lungs. Sooner or later a large number of patients so operated upon develop malignant lesions in the lung.

Finally, the clinical picture of bronchiogenic carcinoma is frequently masked by the complications.

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On Feb. 12 thoracentesis was done, with the puncture site between the third and fourth ribs in the posterior-right side. No fluid was obtained.

Punch biopsy was done into the mass on Feb. 25. A few shreds of tissue were obtained, the microscopic report of which was negative for carcinoma. It was then decided that an open thoracotomy should be done to see if the density was due to an abscess. A portion of the third rib was removed posteriorly and biopsy taken of the pleura and attached lung. This was examined microscopically and the section showed mostly fibrous tissue in which there were areas of round-cell infiltration. This can be interpreted as thickened pleura. There was one small piece of lung tissue in which there was considerable atelectasis and the few remaining alveoli were filled with phagocytic cells and blood pigment. No evidence of neoplasm was seen in any of the sections at hand. The patient became weaker and finally died at his home on Jan. 20, 1938. An autopsy revealed the following: The pleural surface of the right lung showed dense, fibrous thickening. The lung was nodular and subrepitant in consistency. The main bronchus to the right upper lobe just distal to its bifurcation was almost entirely occluded, except for a minute lumen of about 1 mm., by a firm mass of cellular, grayish-white tissue which appeared to rise from the mucosa and which infiltrated into the adjacent lung substance for a distance of about 3 cm. The branches of this bronchus distal to the point of obstruction were dilated and showed a necrotic reddish-purple surface.

Microscopic examination.—Sections from the main mass of the tumor described grossly showed very extensive necrosis of the tumor about the periphery. There were frequent clusters of viable tumor cells. These were arranged in irregular clusters and strands and solid, cellular cords. In many places large areas of tumor tissue were necrotic, except at the very periphery where there were viable tumor cells. Generally the tumor cells were small and undifferentiated. They formed frequent epithelial pearls in places, although it was not possible to demonstrate intracellular bridges in these areas and it was questionable whether these were active epithelial pearls or areas of beginning necrosis. Their appearance and the fact that the tumor remained so well confined to the lung suggested that these were true squamous epithelial pearls. Adjacent and supporting connective tissue showed very dense hyaline fibrosis.

Comments.—The clinical history, symptoms, and signs all pointed to carcinoma: loss of weight, edema, hemoptysis, cough, severe pain, and x-ray. Yet, at no time, in spite of biopsies being made, even with rib resection, was carcinoma positively diagnosed. This case is described to show how, with all means at our command, the final diagnosis at times is made only at autopsy, although clinical signs may be so definite that the patient can be treated as having carcinoma of the lung.

SUMMARY AND CONCLUSIONS

The clinical picture of carcinoma of the lung is still so varied that no definite pattern has been discovered to fit the many types of pathologic conditions present. However, with close observation of the patients and

coordinated movement of x-ray tube and film during the x-ray exposure, with the result that a predetermined layer in the body can be radiographed to the more or less exclusion of the structures lying above or below the layer under examination. There are five major types of apparatus invented for this purpose, and there have been simple modifications of some of them. Because of the multiplicity of methods, a general term to include all of them should be used. For this reason, I have strongly urged body-section radiography as the general, inclusive term. It is equally urged that the specific terms be restricted to the particular type of apparatus or principle used. The specific terms used for this method of radiologic examination, in the order of their appearance in the literature, are: stratigraph (Vallebona¹), planigraph (Ziedses des Plantes²), tomograph (Grossmann³ and Chaoul⁴), lamina-graph (Kieffer⁵ and Moore⁶), and the biotome of Bocage.⁷

Bocage was the discoverer of the underlying principle of body-section radiography. As far as I can determine, he did not publish a description of his apparatus until 1938. He recommends that an inclusive term be used to cover all the methods of this type of radiographic examination. For this general term he uses the word *radiotomie*, Anglicized to radiotomy, because of its etymological correctness. I agree with Bocage and consider that the Anglicized form, radiotomy, is superior to any other term so far suggested.

There are also several improvisations for imparting coordinated movement of tube and film for this type of examination. To me it seems unfortunate that the terms planigraphy and tomography are used to describe not only the improvised modification of the principle, but also types of apparatus other than the tomograph or planigraph. In fairness to the investigators in this field of radiography, the indiscriminate use of specific terms for a particular piece of apparatus or method should not be employed to describe another type of apparatus or method from which it radically differs.

In all methods of body-section radiography there is the same objective in view. This is to disperse overlying and underlying shadows and leave a selected layer in the body relatively unobstructed. Another objective is to visualize as thin a layer as possible because minimal contrast in density in such a layer can be brought out. This is called the depth of focus of the apparatus. As a general rule, the more compound the movement of tube and film during exposure, the more efficient the dispersion of unwanted shadows. With simple attachments to standard equipment, body-section radiographs can be made with considerable success. However, the radiographs are inferior to those produced with apparatus of mechanically superior type.

It is not proposed to describe the different types of apparatus used for body-section radiography or to discuss the mechanical and mathe-

BODY-SECTION RADIOGRAPHY IN MALIGNANCY OF THE LOWER RESPIRATORY TRACT

SHERWOOD MOORE, M.D., St. LOUIS, Mo.

(From the Edward Mallinckrodt Institute of Radiology, Washington University School of Medicine)

CANCER of the lung is of more frequent occurrence than is generally supposed. It comprises from 5 to 10 per cent of all cancers and is about equal in incidence to cancer of the rectum. In fifteen years in the Chest Service of the Washington University Medical School there have been 400 cases of bronchiogenic carcinoma.

An unfortunate feature of pulmonary cancer is the fact that in the neighborhood of 85 per cent of the cases are advanced and, from the therapeutic standpoint, practically hopeless, because of distant metastases, such as to the supraclavicular lymph nodes, brain, pleural implantations, mediastinal involvement indicated by paralysis of the recurrent laryngeal, or phrenic nerves. Under these conditions radiation treatment offers little except palliation, and surgery, nothing.

With the rapid development of thoracic surgery of the past few years, surgical excision by lobectomy or pneumonectomy can be carried out for pulmonary cancer with brilliant results, providing a sufficiently early diagnosis has been made. As a choice between radiation treatment of early cancer of the lung and its surgical excision, there can be but one, and that is excision. Taking all types of cases of the surgical attack on pulmonary carcinoma, the mortality rate is in the vicinity of 30 per cent of the cases operated upon, and results are steadily and constantly improving. In ten successive examples of pneumonectomy and lobectomy for pulmonary carcinoma there was only one operative death. Operative technique has improved to the point where the hospitalization and postoperative care are being constantly bettered, and the patient is being restored to his normal occupation in a shorter time than previously. It has been stated that approximately 65 per cent of all cases of intraluminal, bronchiogenic carcinoma can be diagnosed and located by symptoms, physical signs, bronchography, and bronchoscopy. This figure seems too high. It may be true for the lower half of the lung, but there could scarcely be such a figure for the upper half. There is no selectivity of location of cancer in these two sectors of the lung. Any means which will aid in the discovery of the early occluding lesions should materially reduce the 35 per cent which cannot be accurately diagnosed by the means mentioned. Body section radiography should reduce the remaining 35 per cent.

The underlying principle of body-section radiography has been developed only in the past few years. It consists in employing a properly



Fig. 2. A, Conventional film of chest. Clinical diagnosis: tumor of left lung. B, Arrows indicate dislocation of trachea shown in laminagraph.



Fig. 1—A, Conventional film of chest. Opacity of left apex. B, Note small bronchial branches visualized in the lambograph. C, Autopsy section of lung shows solid, carcinomatous mass with absence of bronchial branches.

(From the *American Journal of Roentgenology* and *Surgery*.)

A.

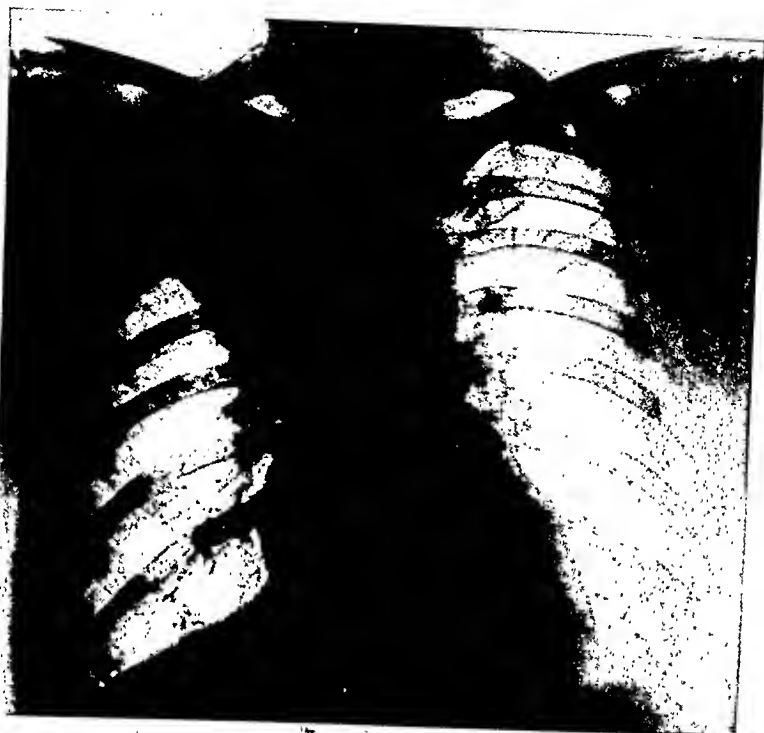


B.



FIG. 1.—A. Conventional film of chest. Massive infiltration, upper lobe of left lung. B. Lumbarograph: Upper arrow points to obstruction of the branch to the upper lobe where it turns posteriorly. Lower arrow indicates lower lobe bronchial branch. Note absence of bronchial branches in opaque area. Unconfirmed.

A.



B.

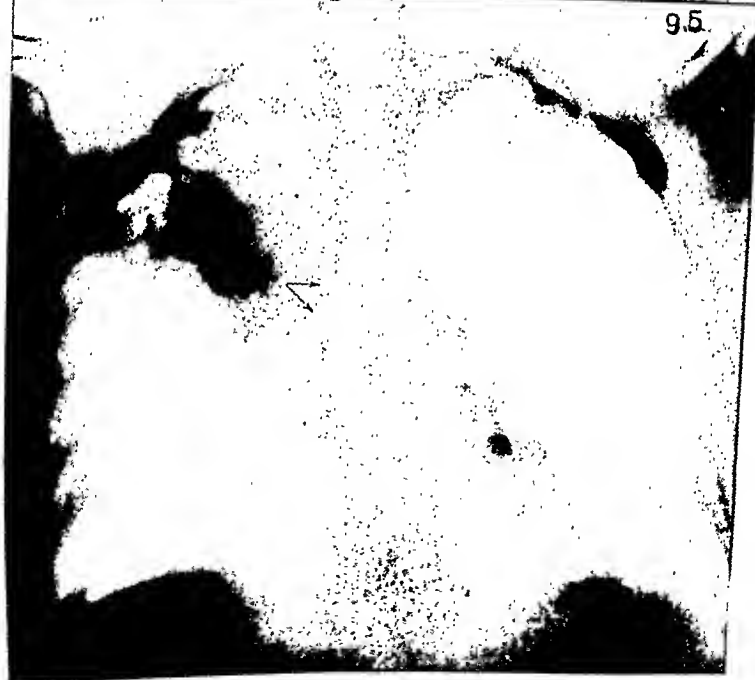


Fig. 3.—A, Conventional film of chest. Opacity of right apex. B, Laminagraph at 9.5 cm. Arrows point to projection into right main bronchus. Note multiple cavitation periphery of opaque area. Bronchoscopic biopsy: Mixed tumor of lung.

matical principles involved. The reader is referred to the publications of Vallebona,¹ Grossmann,³ Chaoul,⁴ Andrews,⁸ Kieffer,⁵ Moore,⁶ Bocage,⁷ and others.

From what has been said, it follows that body-section radiography is of greatest use anatomically where there is a maximum superimposition of structures and, on the contrary, is of least value when the oppo-

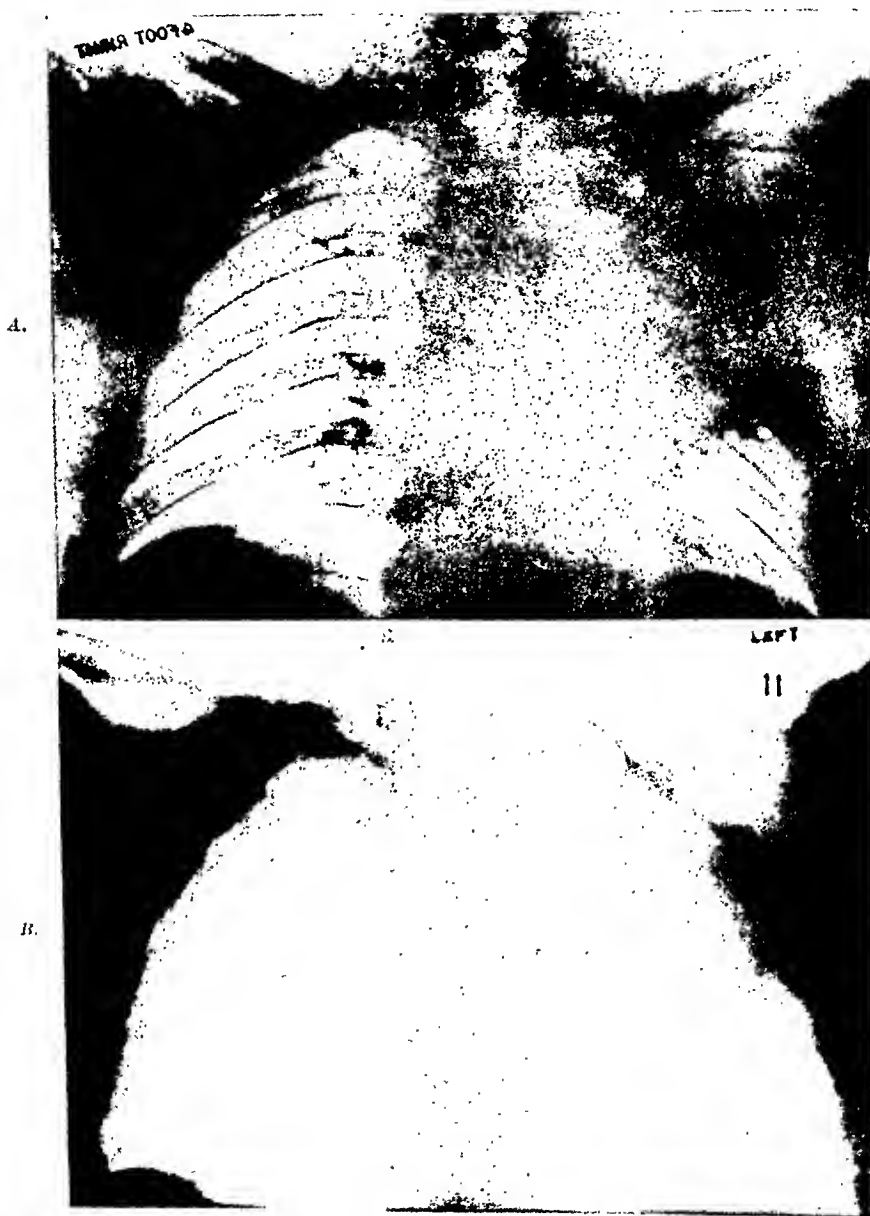


FIG. 6. —A. Conventional bronchography. Incomplete filling of the upper lobe branches. B. Laminagraph. Termination of left main bronchus with distal atelectasis. Bronchogenic carcinoma confirmed by operation.



Fig. 5.—A, Conventional bronchography. Incomplete filling of bronchial branches to upper lobe. B, Laminagraph. Arrow indicates point of narrowing of bronchial branches. Confirmed by autopsy. (From the *American Journal of Roentgenology and Radium Therapy*.)

amination that it may discover malignancy where other methods, such as bronchography and bronchoscopy, or a combination of the two, have failed. The method has been of particular value in the upper portions of the lungs which are always difficult to examine by bronchography and are inaccessible to the bronchoscope. It should be said that body-



Fig. 8.—A. Suspected mediastinal tumor in the left hilus; B. laminagraph identifies the suspected tumefaction as the left pulmonary artery.

site is the case. Also, its maximum value would be where there is the minimum amount of density contrast present in the layer under investigation. This applies in pathologic states if a pathologic process produces unwanted shadows which obscure the region under investigation or the process is one which produces only minimal contrast in density.



Fig. 7.—A, Conventional film of chest. Area of atelectasis in the lung. Arrow indicates termination of bronchus to atelectatic area. B, Arrow indicates excavation in the lung. Bronchiogenic carcinoma confirmed by autopsy.

Body-section radiography is of the greatest value in the examination of the respiratory tract. All investigators report it of value in infectious processes of chronic nature of the respiratory tract, particularly in the lungs. The evidence indicates that it is of equal value in neoplastic disease. There is the further advantage of this method of ex-

amination that it may discover malignancy where other methods, such as bronchography and bronchoscopy, or a combination of the two, have failed. The method has been of particular value in the upper portions of the lungs which are always difficult to examine by bronchography and are inaccessible to the bronchoscope. It should be said that body-

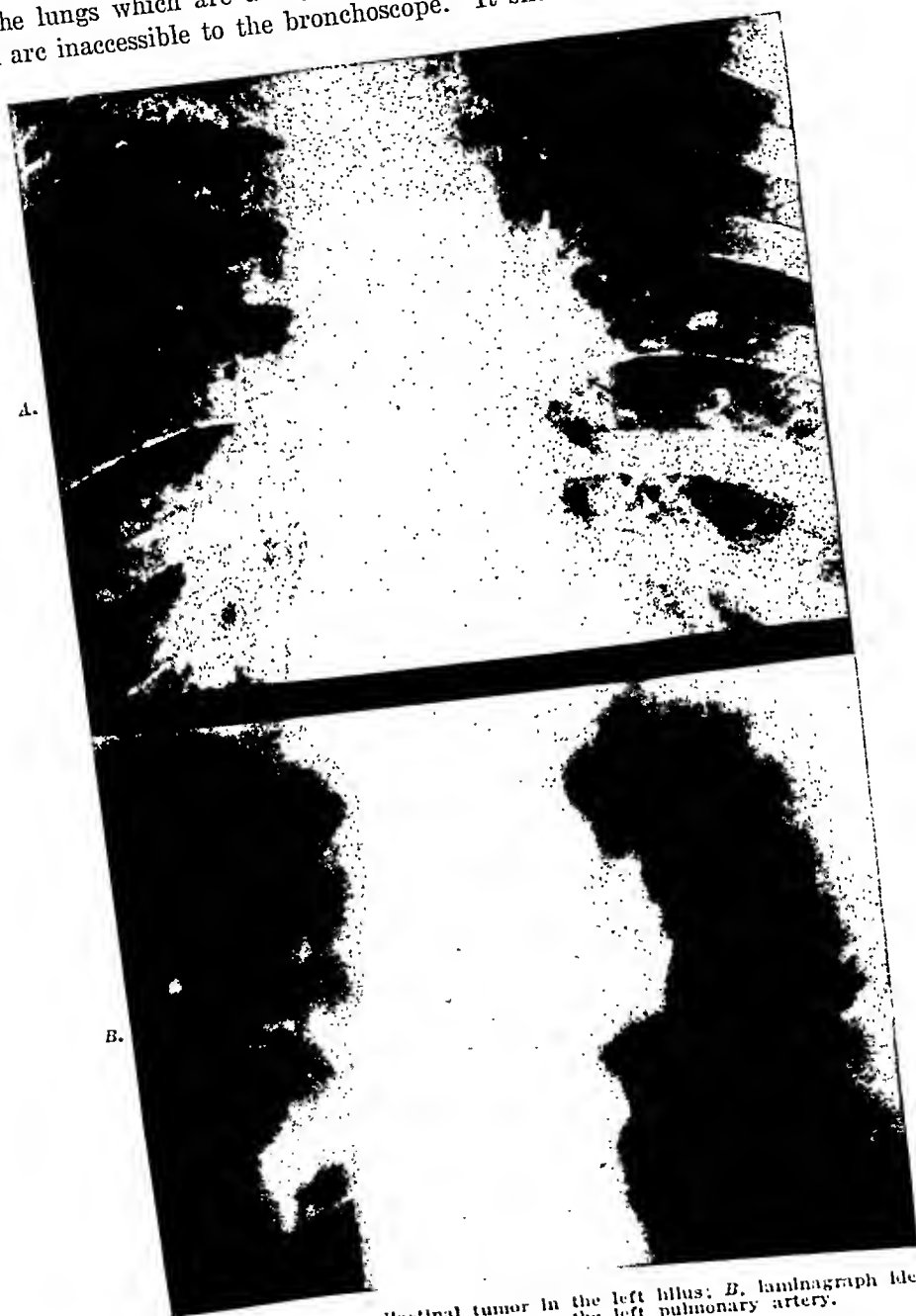


Fig. 8.--A. Suspected mediastinal tumor in the left hilus; B. laminagraph identifies the suspected tumefaction as the left pulmonary artery.

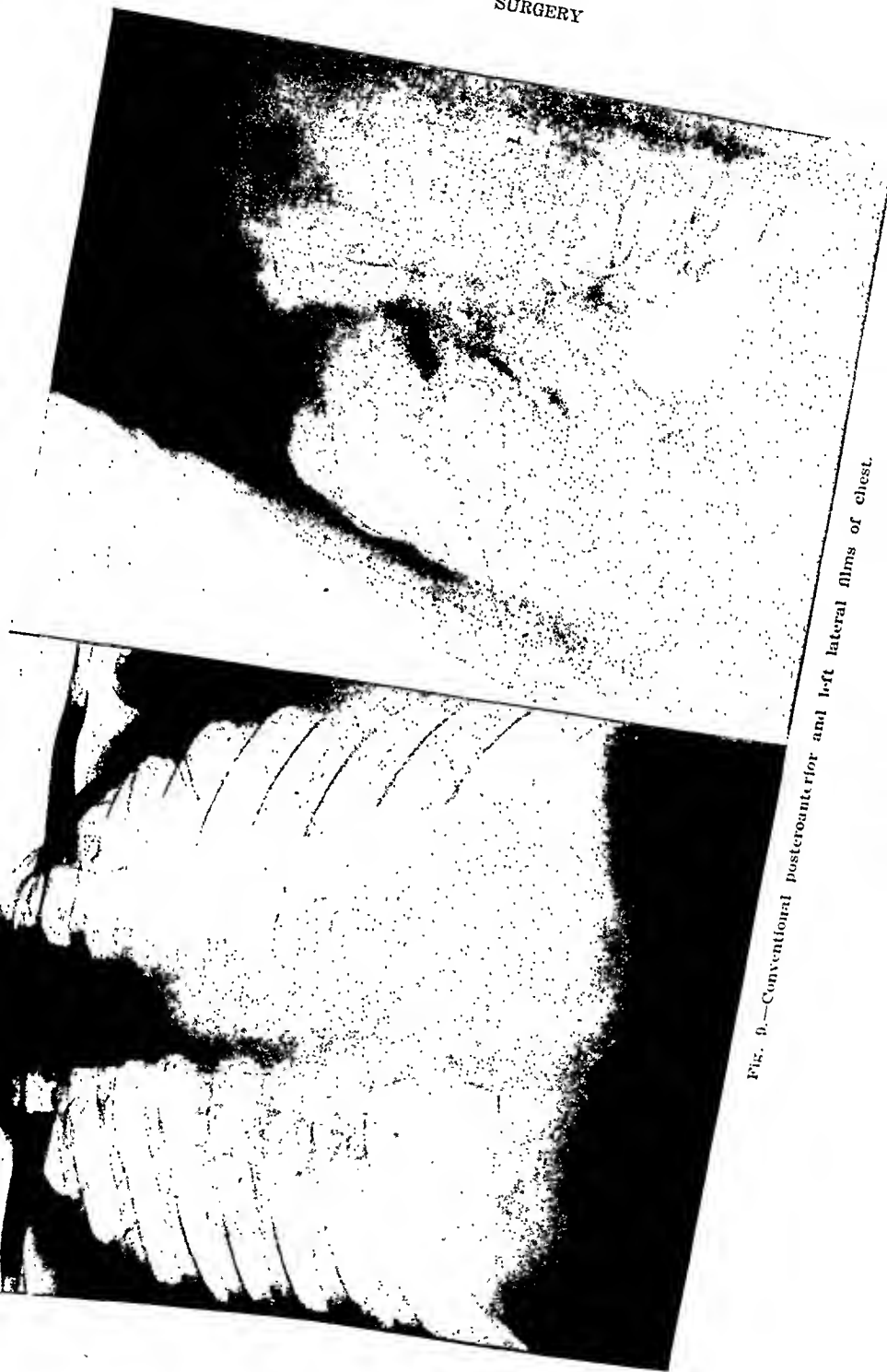


Fig. 9.—Conventional posteroanterior and left lateral films of chest.

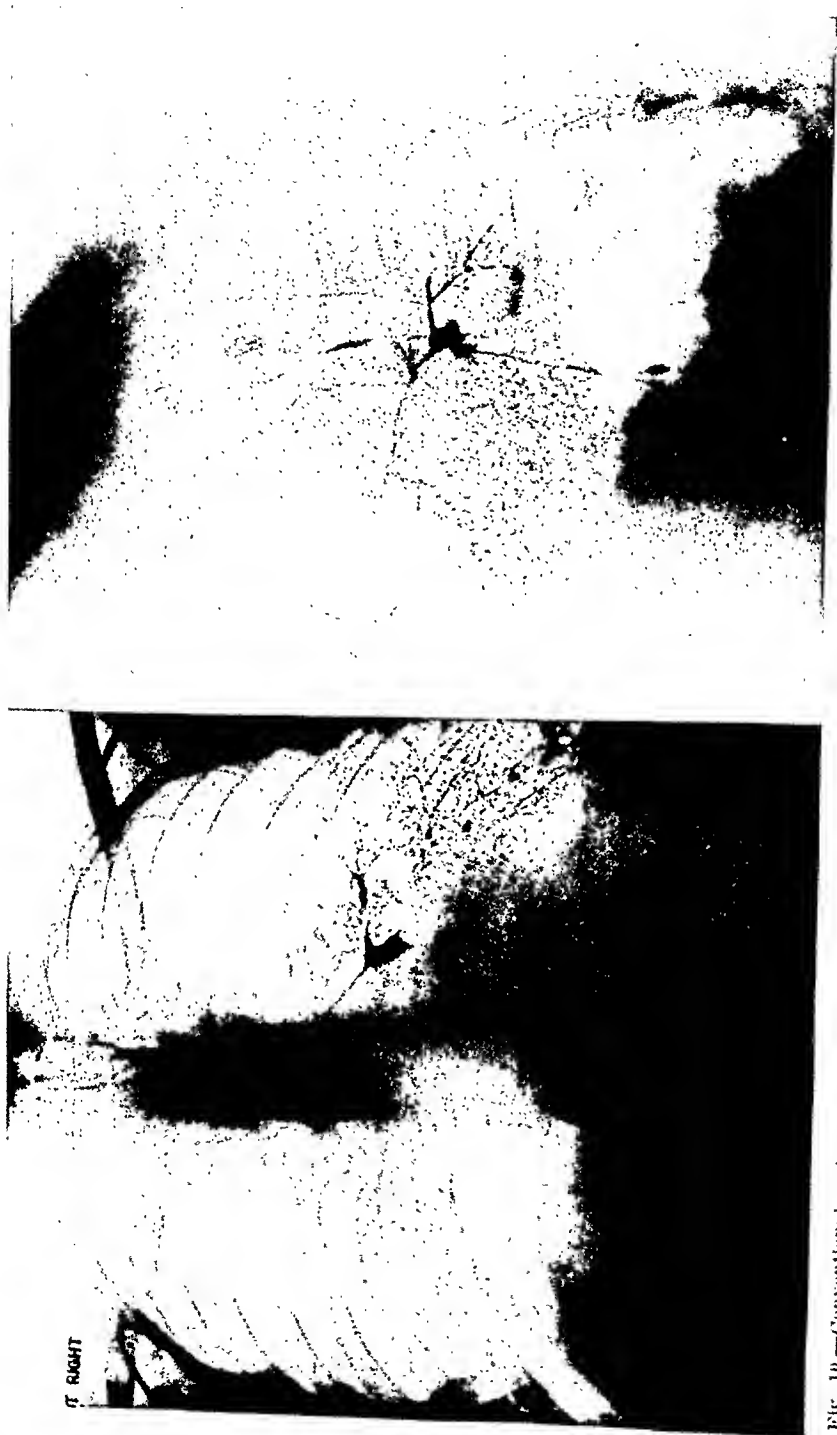


Fig. 10.—Conventional posteroanterior and left lateral bronchography of same patient as shown in Fig. 9. Note termination of descending bronchial branch.

section radiography does not supersede these methods of examination but should be considered as complementary to them.

Laminagraphic examination of the lower respiratory tract can be invaluable in cases where other methods of examination are negative or inconclusive. This presupposes a standard radiographic examination. The suspected area is measured from the film or estimated under the fluoroscope, and a series of laminagrams is made in a ventrodorsal or dorsoventral position, depending on which will put the suspected area nearest the film. For a lateral view, if it is desired, the patient is placed on the side which will bring the lesion nearest the film. Our practice has been to make films at each centimeter of depth through the suspected area. It should be said, incidentally, that the lateral projection is chiefly useful in the investigation of the mediastinum.



Fig. 11.—Laminagraph of same patient as shown in Fig. 9 clearly shows area of infiltration in left lung. Bronchogenic carcinoma confirmed by lobectomy.

The laminagraph can clearly reveal the tracheobronchial tree, and bronchial branches as small as 3 to 4 mm. in diameter have been shown (Fig. 1). Dislocation (Fig. 2), impingement or distortion (Fig. 3), and termination through obstruction (Figs. 4, 5, and 6) have been clearly shown. It is occasionally possible, by varying the exposures, to separate the vascular and the respiratory tree, but this has not been



A.

Fig. 12.—A, Conventional film of chest. Arrows indicate outline of tumor not visualized on the lateral film. B, Lateral lamina graph of chest about at the midline indicates clear-cut tumor mass. Exploratory operation: Tumor mass proved to be an aneurysm of a ductus arteriosus.

B.

Exploratory operation: Tumor mass

done with any great consistency. Intraluminal obstruction from tumor with atelectasis distal to the point of obstruction has been clearly shown. In cases where carcinomatous infiltration has been diffuse, absence of bronchial branches has been shown, and dislocation of branches in the adjacent, healthy lung has also been revealed (Fig. 1). Of course, this applies to what may be termed early cases, or rather, those in which suppuration and abscess formation have not occurred. Very early excavation through abscess formation has been shown in an area of atelectasis in a case of bronchiogenic carcinoma confirmed by autopsy (Fig. 7). Perihilar increase of density, thought to be due to pulmonary tumor, has been shown to be of vascular origin (Fig. 8). Narrowing of a main bronchus through an inflammatory process in its wall has been shown and confirmed by bronchoscopic biopsy. An early bronchiogenic carcinoma (Figs. 9, 10, and 11) confirmed by lobectomy has been shown when there was some doubt following bronchography.

Mediastinal tumors or those near the midline have their true location and their point of origin revealed with suitably made laminagrams. Occasionally in certain standard films of the mediastinum, when a malignant tumor was thought to be present, the laminagraph has revealed an entirely different structure (Fig. 12).

In approximately two years' time there have been ninety-nine tumors of the lower respiratory tract. Of these, twenty-six have been investigated with the laminagraph, the aid from which has been invaluable. There is every reason to suppose that, with growing experience with this method of examination, far earlier diagnoses of malignant tumor of the lower respiratory tract can be made to the consequent benefits of these unfortunate patients.

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BRONCHOSCOPIC DIAGNOSIS OF BRONCHIAL CARCINOMA

PAUL HOLINGER, M.D., CHICAGO, ILL., AND DAVID B. RADNER, M.D.,
HONOLULU, HAWAII

*(From the University of Illinois College of Medicine and St. Luke's Hospital,
Chicago, Ill.)*

PRIMARY carcinoma of the bronchus has been diagnosed with rapidly increasing frequency during the past decade. Available evidence demonstrates that, although there is an actual increase in the frequency of this disease, accuracy of diagnosis, made possible by the roentgen ray, the bronchoscope, and thoracic surgery, also emphasizes an apparent increase in incidence.¹⁻³ The bronchoscopic diagnosis of bronchogenic carcinoma is based upon the interpretation of pathology revealed by a direct inspection of the tracheobronchial tree. Thus the bronchoscope is merely a tracheal and bronchial speculum, permitting visual or instrumental examination of otherwise inaccessible portions of the air passages. The purpose of bronchoscopy as an aid in the diagnosis of bronchogenic carcinoma is fourfold: (1) to study the character of the lesion; (2) to note accurately its location and determine its extent along the bronchial walls; (3) to secure tissue for biopsy and thus reveal the exact nature of the growth; and (4) to aid in determining operability by noting evidence or lack of evidence of metastases. These points will be discussed in detail later.

The indications for inspection of the tracheobronchial tree can be listed symptomatically or by the types of pathology elicited by physical examination or x-ray. No physical signs are diagnostic or even characteristic of new growth,⁴ but the most frequent symptoms, cough, hemoptysis, or a wheeze, demand thorough investigation to determine the character of the underlying pathology. Obviously, since symptoms depend upon the location and extent of the lesion, they may be entirely absent, as in a very small early lesion on the wall of a major bronchus. Or they may be extensive and still be caused by a relatively small lesion obstructing a major bronchus. As Ochsner and DeBakey¹ state: "There are few or no symptoms in the early course of bronchial carcinoma. . . . Generally, the symptoms are not produced by the neoplasm itself, but are due to secondary changes resulting from its presence."

When roentgen findings suggest bronchial obstruction, otherwise unexplained areas of pneumonitis or gross suppuration, the indication for bronchoscopy is obvious. As Jackson and Konzelmann⁵ state, bronchial obstruction is the most cardinal indication for diagnostic bronchoscopy. According to various studies,^{6, 7} over 80 per cent of the neoplasms originate in the major bronchi, and it is significant to note the earliest symptoms will not be accompanied by signs of bronchial obstruction which

could be demonstrated roentgenologically. Westermarck⁸ says that "cancer of the bronchus does not show directly in the roentgenograms until it is in a very advanced stage." Bronchoscopic examination, therefore, is indicated when symptoms of an unexplained cough, hemoptysis, or a wheeze are present in spite of a negative roentgen examination.^{9, 10} Only in this manner can an early diagnosis be made. To wait until the suspicion is confirmed more positively roentgenologically or by means other than direct inspection results in a diagnosis established too late to aid the patient.

Pulmonary suppuration is the second most constant finding associated with an endobronchial neoplasm. The suppuration, in fact, is frequently so predominant that the neoplasm may be entirely overlooked. Findings of a drowned lung, single or multiple lung abscesses, or bronchiectasis are often secondary manifestations of a bronchogenic carcinoma, caused not only by the erosion of the neoplasm, but more frequently by the bronchial obstruction.

Hemoptysis requires as thorough a search for its source as is made by the urologist in cases of hematuria. Gross hemoptysis, of course, definitely contraindicates bronchoscopy. In early lesions with only occasional streaking of sputum, however, the small stream of blood may be followed to its source to reveal the location of the neoplasm. Peripheral tumors may be revealed symptomatically only by occasional slight hemoptyses, vague chest discomfort, or pain due to pleural irritation.

The indispensability of the bronchoscopic examination in all cases of suspected bronchogenic carcinoma and of obscure pulmonary pathology is now well recognized by internists and surgeons. The accuracy of tissue diagnosis and the information gained to determine the operability of the tumor stimulate the bronchologist to study the lesion from a number of aspects.

Character of the Lesion.—Jackson¹¹ pointed out that there are three types of tumors which manifest themselves by bronchial obstruction: (a) endobronchial, the tumor itself hanging free in the bronchial lumen; (b) peribronchial, the tumor producing a thickening of the bronchial wall, thus producing obstruction; and (c) extrabronchial with endobronchial intrusion, the tumor compressing the bronchus to occlude it partially or completely.

All three types of tumors produce identical symptoms of bronchial obstruction. They manifest themselves physically or roentgenologically by a wheeze, obstructive emphysema, or atelectasis, and direct inspection is necessary to study the character of the growth. These findings are identical to those produced by foreign bodies in the tracheobronchial tree and briefly might be mentioned.

If the lumen of a bronchus is constricted partially, by an intrabronchial growth or by extrabronchial compression produced by a tumor, and air can pass the obstruction on inspiration and expiration, x-ray

findings are negative. On physical examination, however, a wheeze is heard at the open mouth and throughout the chest and is loudest over the point of obstruction. As the tumor grows, the obstruction increases and air becomes trapped in the portion of lung distal to the obstruction, due to the slight increase in the diameter of the lumen of the bronchus on inspiration, which permits air to pass the obstruction. On expiration, the bronchial wall collapses around the tumor, whereby air cannot leave that portion of the lung. The roentgen picture then is negative if the film is taken, as most are, at deep inspiration. A film taken during complete expiration, however, shows a marked shift of the heart and mediastinal structures away from the side of the lesion and a stationary depressed diaphragm on the affected side.

Complete occlusion of the bronchus by the tumor results in atelectasis as the air is absorbed beyond the obstruction. The heart and mediastinum are displaced toward the lesion as they are drawn into the dense atelectatic area to produce the characteristic picture.

Location of Growth and Extent Along Bronchial Walls.—Physical examination and roentgen technique have become so accurate that the exact location of a bronchogenic carcinoma is made frequently prior to direct visualization of the tumor. This diagnosis is reached by determining the degree and extent of bronchial obstruction. Endoscopically, however, the tumor often is found invading the bronchial walls far above the point of complete obstruction. This may be determined only by direct visualization.

Biopsy.—The most important function of the bronchoscope in establishing the diagnosis of bronchogenic carcinoma is the obtaining of tissue for biopsy. Sufficient tissue in the majority of cases can be removed with forceps to permit satisfactory study and classification of the tumor. In this manner an increasingly high percentage of cases is correctly diagnosed. In a series of 300 cases, Kramer and Som¹² proved the diagnosis by bronchoscopic biopsy in 222, or 74 per cent. Clerf¹³ obtained a positive tissue diagnosis in 98, or 68.5 per cent, of 143 proved cases of bronchogenic carcinoma. In Jackson's¹⁴ statistics bronchoscopic biopsy was possible in about 75 per cent of the cases of bronchial carcinoma, and Overholt¹⁰ obtained a specimen for microscopic study in 28 of the 32 cases of his series.

The bronchoscopic picture is extremely variable. In early lesions a small stream of blood may lead to an eroded area from which tissue may be removed to reveal the identity of the tumor. The blood itself is aspirated, collected, centrifuged, fixed, and sectioned. It occasionally establishes the diagnosis when the tumor itself is too small or too deep in the periphery to be reached with forceps.

More frequently, however, the bronchoscope demonstrates a verrucous, friable, soft mass completely obstructing the lumen of one of the main bronchi. It occasionally is covered with exudate. Tissue easily can be

teased off this mass with forceps used for removing ball bearings or beads from the air or food passages.⁵ These forceps are preferred to the sharper cutting type because they cause less bleeding. Should the tumor be very firm or infiltrated, there is no contraindication to the use of the cutting or tissue-biopsy type of forceps.

The more advanced type of lesion is accompanied by copious quantities of sanguinopurulent secretion. The bronchi are distorted, the walls irregular and freely bleeding, and the true obstruction is a friable mass. Large pieces of tissue can be removed for biopsy and the patient relieved temporarily by aspiration of the putrid material beyond the obstruction. In these cases, however, as Lederer¹⁵ suggests, the element of danger from hemorrhage must be kept in mind. Occasionally at this stage the destruction of tissue confuses the picture by profuse bleeding, pus, and granulation tissue. Repeated bronchoscopies may be necessary to get tissue representative of the tumor itself and not alone of the peripheral inflammatory zone⁵ to establish the diagnosis.

Special endoscopic problems arise from tumors in the upper lobe bronchi. Should an atelectasis of an entire upper lobe occur, the tumor in many instances protrudes from the upper lobe orifice. As the upper lobe bronchus leaves the main bronchus on the right side at an angle of 90 degrees and on the left side at about 70 degrees, however, a tumor 1 cm. within the orifice seldom can be inspected directly, especially because the bronchial walls are made rigid by neoplastic involvement and in many instances will not permit gentle manipulation with the lip of the bronchoscope to give adequate exposure. These angles, furthermore, are made more acute if the lobe beyond the point of obstruction is atelectatic, thereby tending to pull the bronchus further toward the apex. Thus other aids, such as an artificially induced pneumothorax, are needed to release the distorted bronchus and bring it further into the direction of the main bronchus, facilitating its entrance with the bronchoscope. This procedure was used by Arbuckle to obtain the biopsy in what later proved to be the first case of successful pneumonectomy for bronchogenic carcinoma.¹⁶

Inspection of the upper lobe bronchi is facilitated further by the use of a retrograde telescope or retrograde mirror. The use of these instruments is hampered by the condensation of moisture on the glass surfaces. By heating them thoroughly first or coating the surfaces with special oils, very satisfactory observations may be made.

Fluoroscopy as an adjunct to the bronchoscopic procedure is routinely used in dealing with certain types of bronchopulmonary foreign bodies. This is especially true in dealing with foreign bodies in the periphery of the lung where the bronchi become so small that the use of bronchoscopes with lumina large enough for direct vision is impossible. Biplane fluoroscopy is then indispensable. Too, it may aid in guiding forceps into the

costophrenic angles or upper lobe bronchi in search of tumor tissue for biopsy when the tumor lies in a branch bronchus beyond the scope of direct vision.¹⁷

Failure to obtain a positive biopsy in cases later proved, either surgically or at post mortem, to be bronchogenic carcinoma frequently may be attributed to the nature of the malignancy. The rigidity of the bronchial tree or the trachea adjacent to a tumor may make it impossible to advance the bronchoscope to the endobronchial portion of the tumor. If the bronchial compression of a tumor collapses a bronchus proximal to the endobronchial invasion of that tumor, biopsy cannot be obtained without danger of penetrating pulmonary tissue. The deformity and rigidity, of course, help indicate the clinical diagnosis of cancer,^{14, 18} and add to the information gained from x-ray and physical examination in establishing the diagnosis.

Aid in Determining Operability.—Bronchoscopy may be repeated if findings of questionable significance present themselves,¹⁹ or if the biopsy reveals no positive tissue. But valuable time should not be lost waiting for endobronchial evidence of a tumor if other features strongly indicate a malignancy.

Besides actually inspecting the endobronchial tumor and noting its character, exact relationship to surrounding structures, and its extent along a bronchial wall, certain features in the bronchoscopic appearance of the remainder of the tracheobronchial tree are of great importance. As Jackson and Konzelmann²⁰ state: "Perhaps a little too much emphasis has been placed upon positive biopsy in the past. Certainly biopsy material, when obtainable, should be carefully studied, but we must not concentrate our attention so closely on biopsy as to neglect the other aspects of the bronchoscopic and clinical picture. If the accessible portions of the tracheobronchial tree are found entirely negative, so much the better; the surgeon knows that in such a case he can amputate any of the larger bronchi and not leave tumor tissue behind, though he must proceed with no knowledge of the histopathologic character of the lesion and rely solely on the clinical diagnosis." Enlargement of mediastinal glands is detected by a thickening at the division of the trachea. This area, the carina, is usually sharp, regular, and freely movable. With mediastinal metastases, the carina becomes thickened, irregular, and fixed. Should these findings be present, lobectomy or pneumonectomy, of course, is contraindicated.

Direct or indirect inspection of the larynx frequently gives valuable correlative information. Hoarseness, produced by a paralysis of the left recurrent laryngeal nerve as it passes under the arch of the aorta, is almost always present in late, left-sided bronchogenic carcinoma. It is not an infrequent early sign and has occasionally been the first symptom of which the patient complains. Paralysis of the right vocal cord, a much less frequent finding, indicates, in cases of apical tumors on the

teased off this mass with forceps used for removing ball bearings or beads from the air or food passages.⁵ These forceps are preferred to the sharper cutting type because they cause less bleeding. Should the tumor be very firm or infiltrated, there is no contraindication to the use of the cutting or tissue-biopsy type of forceps.

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diathermy. Vinson and Bowling²⁴ first described the value of this type of therapy which, in certain selected cases, is of definite value in the treatment of primary carcinoma of the bronchus.^{14, 25, 26}

A more recent type of endobronchial therapy directed bronchoscopically is the implantation of radon seeds or radium directly into the obstructing tumor. Although the results have been palliative in most instances, a few exceptions should be mentioned. Negus,²⁷ Kernan,²⁵ Ormerod,²⁸ and others have reported clinical cures by the use of this method together with the use of surgical diathermy. It should be noted that in most of these cases the biopsy revealed the tumor to be an adenocarcinoma.

The bronchoscopic insertion of tubes containing radon has been suggested by Soulas,²⁹ von Eicken,³⁰ Negus,²⁷ and others. More recently, Pressman and Emery³¹ have devised an applicator for the implantation of radium needles directly into the bronchus to remain in place thirty to sixty-five hours. A preliminary pneumothorax was of definite advantage in this latter type of therapy.

Clinical cures of bronchogenic carcinoma through the use of any or all of these bronchoscopically directed methods of therapy are significant and frequent enough to suggest their use in selected cases otherwise inoperable.

CONCLUSIONS

1. The purpose of bronchoscopy as an aid in the diagnosis of bronchial carcinoma is fourfold: (a) to study the character of the lesion, (b) to note its location and extent along the bronchial wall, (c) to secure tissue for biopsy if the tumor can be visualized, and (d) to aid in determining the operability of the tumor.

2. Bronchoscopic examination of the tracheobronchial tree is an indispensable aid in establishing the differential diagnosis of pulmonary pathology.

3. The treatment of bronchogenic carcinoma, primarily surgical in suitable cases, may be carried out endoscopically in certain instances by the use of electrocoagulation, radon, or radium implantation. Although several recoveries have been reported by these methods, they are, for the most part, palliative.

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right side, that invasion or compression has progressed to a point under the right subclavian artery. This again corroborates evidence of extension.

Another important role of bronchoscopy in relation to bronchogenic carcinoma is the establishing of the differential diagnosis. Any type of bronchial stenosis, whether produced by tuberculosis, foreign bodies, or bronchiectasis must be considered.²¹ An inflammatory lesion, such as a lung abscess, may be accompanied by marked proliferation of granulation tissue. Bronchoscopically removed tissue from this area is the only method of establishing whether the abscess is secondary to a carcinoma or is entirely inflammatory in character.

Tuberculosis, often most difficult to diagnose, especially in its incipient stage, may produce symptoms of cough, hemoptysis, and loss of weight which are sufficient to make the diagnosis of tuberculosis, in spite of a negative chest x-ray or sputum examinations repeatedly negative for tubercle bacilli. Bronchoscopically aspirated secretion may show the bacilli, but, what is more important, an early carcinoma may be discovered. Only by making early differential diagnoses can cases favorable to surgery be discovered.

Benign tumors of the bronchus offer another problem in diagnosis which can be settled only by microscopic examination of the tissue. The bronchoscopic appearance of a benign lesion is frequently quite characteristic, but, as in dealing with any tumor, the gross appearance can be relied upon only in a small percentage of cases.

Bronchoscopic Therapy.—A remarkable disproportion exists, as Clerf¹³ states, between the large number of reported cases of primary carcinoma of the bronchus and the small group that has been successfully treated. The surgical excision of a carcinoma is recognized as the therapeutic procedure of choice when feasible. The growing list of patients treated successfully in this manner represents a surgical advance only in the experimental stage a little more than five years ago. Certain endobronchial tumors fall into a borderline classification that, though histologically frequently reported as carcinomatous, clinically reacts as benign growths. The bronchoscopic treatment of these tumors, as well as frank malignant growths otherwise inoperable, initiated an interesting phase of bronchology directed toward the re-establishment of the bronchial lumen and efforts to keep it patent.

Forceps removal of a benign bronchial tumor was described first by von Eicken in 1907.²² Later Jackson²³ removed a tumor from the right main bronchus by the same method. The tumor removed by von Eicken was considered benign; that removed by Jackson was regarded, pathologically, as malignant. The forceps removal of tissue obstructing a bronchus is a practical, rapid method of re-establishing the lumen. The control of hemorrhage is difficult with this technique, however; consequently, it has been supplanted to a large degree by the use of surgical

DIAGNOSIS OF MALIGNANT LUNG TUMORS BY ASPIRATION BIOPSY AND BY SPUTUM EXAMINATION

LLOYD F. CRAVER, M.D., NEW YORK, N. Y.

(From the Memorial Hospital)

A CARDINAL principle today in the treatment of malignant tumors is that a biopsy demonstrating the presence of a malignant tumor should be obtained if possible before radical treatment is instituted. In the case of certain deeply situated tumors it may be difficult by ordinary means to secure a biopsy. Cancer of the lung furnishes an example of the difficulties which a clinician may encounter when he wishes to obtain histologic proof of the malignant nature of a tumor before subjecting the patient to radical treatment.

To those who have had a true cross-sectional experience in diagnosing cancer of the lung, it is perfectly obvious that histologic proof is the only proof of this disease. There is no roentgenologic or bronchoscopic appearance that in itself can be claimed to be pathognomonic of cancer of the lung. A strong suggestion, or even a near certainty, of a diagnosis of cancer of the lung, based on the appearance of routine roentgen films, tomograms, lipiodol films, or fungating ulcerated lesions seen through the bronchoscope, cannot compare with the assurance gained by identifying cancer on a microscopic slide, when it comes to deciding for or against pneumonectomy or intensive roentgen therapy. Either the modern surgical or the modern radiological treatment of cancer of the lung is such a radical procedure, and so hazardous to the patient, that it should not be undertaken without good evidence of its necessity.

A belief that early diagnosis of a very high proportion (90 per cent) of primary carcinomas of the lung should be possible by means of the bronchoscope can only reflect an experience that is one-sided and that has missed some aspects of the disease. There is even a considerable group of bulky hilar or mediastinal tumors, primarily bronchiogenic, which on routine roentgen examination would seem to offer every likelihood of positive bronchoscopic biopsies, yet which may present completely negative findings bronchoscopically. There is certainly a large group of primary bronchiogenic carcinomas, increasingly recognized now, in which the lesion lies far out in the lung field or in the upper lobe, beyond accessibility for bronchoscopic biopsy.

Confronted with such examples of bronchoscopically inaccessible lung tumors, the thoracic surgeon in general is inclined to explore through a thoracotomy. This procedure requires admission of the patient to a hospital and subjects him to the risks of a major operative undertaking.

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TABLE I
CARCINOMA OF LUNG FILE, MEMORIAL HOSPITAL

| YEAR | UNPROVED CASES | PROVED CASES | TOTAL |
|------------------|----------------|--------------|-------|
| 1918 | 4 | 0 | 4 |
| 1919 | 8 | 0 | 8 |
| 1920 | 5 | 1 | 6 |
| 1921 | 9 | 1 | 10 |
| 1922 | 16 | 0 | 16 |
| 1923 | 6 | 1 | 7 |
| 1924 | 5 | 3 | 8 |
| 1925 | 14 | 1 | 15 |
| 1926 | 13 | 1 | 14 |
| 1927 | 9 | 2 | 11 |
| 1928 | 17 | 3 | 20 |
| 1929 | 9 | 2 | 11 |
| 1930 | 9 | 8 | 17 |
| 1931 | 15 | 10 | 25 |
| 1932 | 21 | 9 | 30 |
| 1933 | 14 | 18 | 32 |
| 1934 | 14 | 20 | 34 |
| 1935 | 13 | 21 | 34 |
| 1936 | 9 | 20 | 29 |
| 1937 | 3 | 21 | 24 |
| 1938 | 9 | 24 | 33 |
| 1939 (to July 1) | 4 | 9 | 13 |
| Totals | 226 | 175 | 401 |

TABLE II
COMPARISON OF USE BY YEARS OF THREE LEADING METHODS OF INTRAVITAM
DIAGNOSIS OF BRONCHIOGENIC CARCINOMA*

| | THORACOTOMY | BRONCHOSCOPY | ASPIRATION BIOPSY |
|------------------|-------------|--------------|----------------------|
| 1920 | 0 | 1 | 0 |
| 1921 | 1 | 0 | 0 |
| 1922 | 0 | 0 | 0 |
| 1923 | 1 | 0 | 0 |
| 1924 | 1 | 1 | 0 |
| 1925 | 1 | 0 | 0 |
| 1926 | 0 | 1 | 0 |
| 1927 | 0 | 1 | 1 |
| 1928 | 1 | 1 | 1 |
| 1929 | 0 | 2 | 0 |
| 1930 | 0 | 4 | 1 |
| 1931 | 0 | 6 | 3 |
| 1932 | 0 | 5 | 3 |
| 1933 | 0 | 11 | 3 |
| 1934 | 2 | 12 | 3 |
| 1935 | 0 | 10 | 9 |
| 1936 | 0 | 8 | 10 |
| 1937 | 0 | 4 | 15 |
| 1938 | 0 | 9 | 13 |
| 1939 (to July 1) | 1 | 4 | 2 |
| Totals | 8 | 80 | 64 |

*It should be noted that only one of the thoracotomies was done at Memorial Hospital. All the rest were done elsewhere, before the patient was referred to this hospital.

Since a large proportion of cases of lung cancer are inoperable as far as lobectomy or pneumonectomy is concerned, the routine practice of thoracotomy to establish a diagnosis of cancer involves major surgery for many patients for whom there can be offered no hope that the surgeon, finding cancer, can then go on and remove the diseased lung. In cases with pleural effusion, thoracoscopy to determine the presence of pleural metastases may be advisable as a relatively minor procedure, safeguarding against an unwise decision to attempt major operative attack on the disease. Examination of sedimented or centrifuged pleural exudates is notoriously unreliable in making a diagnosis of cancer of the lung. A biopsy of a swollen lymph node may show that the patient has a primary carcinoma arising somewhere within the drainage area of that node, but it is almost the rule that the pathologist cannot determine certainly whether the structure means origin from lung. In rare instances the patient may cough up a piece of tissue that will furnish proof of bronchiogenic carcinoma.

In view of the foregoing premises, and in view of our experience in other fields with the successful practice of aspiration biopsy, the staff at Memorial Hospital began over a decade ago to apply aspiration biopsy to the field of lung tumors, feeling that in this procedure we possessed a means of obtaining a diagnosis quickly, with comparatively little discomfort or danger to the patient, and particularly without subjecting inoperable cases to a major operation, thoracotomy.

A recent survey of our files for carcinoma of the lung yielded 175 cases regarded as proved histologically, from a total of 401 cases (Table I). It is probable that most of the 226 unproved cases were cases of carcinoma of the lung, too, but in them histologic proof is lacking.

In Table I it will be noted that after 1932 the number of proved cases for the first time, and steadily thereafter, exceeded the number of unproved cases. While this increase in proportion of proved cases no doubt in some measure has been due to improved use of the bronchoscope, in probably a larger measure it has been due to increased familiarity and success with the technique of aspiration biopsy. This statement may be illustrated by Table II, which compares by years the use of the three leading methods of obtaining in our series a diagnosis of cancer of the lung, these methods being thoracotomy, bronchoscopy, and aspiration biopsy.

In Table II it will be noted that, beginning with one case in 1927 and with increased frequency since 1934, it has appeared necessary to resort to aspiration biopsy to obtain the diagnosis.

In Table III is presented a summary of the methods relied upon for diagnosis in preparation for treatment in the 175 cases in our series regarded as proved cases of bronchiogenic carcinoma. These methods are listed in the order of likelihood of certainty of proof.

lesion as being unilateral, a straight lateral view, with the film on the affected side, is made at the same time. A preliminary fluoroscopy may be of considerable aid in determining which views to make, and barium swallowing may be indicated in some cases to aid in ruling out esophageal primary lesions; in demonstrating external pressure on the esophagus by a tumor of the lung; or to aid in excluding aneurysm, cyst, or other causes of intrathoracic tumefaction.

If the lesion as portrayed roentgenologically seems not entirely inconsistent with bronchiogenic carcinoma and the history and physical findings also lend support to that diagnosis, the usual next step is bronchoscopy. We now usually prefer to do bronchoscopy in all cases suspected in any way of being cases of cancer of the lung, even though the appearance of the films may not make it seem likely that the lesion will be accessible to the bronchoscope. We do so because occasionally, even in such cases, the bronchoscopist may obtain a positive biopsy, or at least may give helpful information about such points as the presence and location of bronchial distortion or fixity or the presence of blood or pus in the bronchial tree. Another motive at present is, frankly, a desire to put on record additional cases of proved cancer of the lung in which bronchoscopy cannot obtain a positive biopsy, in order to be able to aid in establishing a better general concept of the problems involved in making a diagnosis.

Naturally, if bronchoscopy yields a positive biopsy, the diagnosis can be regarded as made with reasonable certainty and aspiration biopsy need not be employed. To give proper credit to bronchoscopy, it must be said that, in general, the positive biopsies so obtained can be interpreted more readily as to grading of degree of malignancy and as to cell type than can be done with the immediate smears of material aspirated from a lung tumor by a needle. On the other hand, however, sectioning of the clot frequently obtained in the process of aspiration biopsy may yield histologic sections of a much better quality than the crushed scrapings which are all that may be obtained in some cases by bronchoscopy, and in some instances these clot sections are indistinguishable from regular sections such as are obtainable by thoracotomy or from autopsy material.

If, as so often happens, despite unimpeachable technique, no positive biopsy can be obtained by the bronchoscopist, we then have to consider whether it is feasible to do an aspiration biopsy. This problem is comparatively easy in the case of bulky peripheral masses, especially those that are well delimited and look solid. In these cases it is easy to select the best site for insertion of the needle, and, in fact one may have a choice of more than one approach. In many other instances, however, more information is needed about the best site for aspiration than is available from routine chest films alone, and this information may have to be built up from several sources. One has first to review

TABLE III

MODES OF INTRAVITAM DIAGNOSIS (IN PREPARATION FOR TREATMENT)
OF 175 CASES OF PRIMARY CARCINOMA OF LUNG

| | NO. OF CASES |
|--|--------------|
| Thoracotomy | 8 |
| Expectorated tissue (added confirmation by this means in 2 cases) | 0 |
| Bronchoscopy | 80 |
| Aspiration biopsy from lung | 64 |
| Aspiration biopsy from rib (directly invaded by the lung tumor) | 1 |
| Excision or aspiration biopsy of lymph nodes (added confirmation by this means in 5 other cases) | 7 |
| No tissue during life (all subsequently confirmed by autopsy) | 15 |
| Total | 175 |

It will be noted in Table III that in 64 cases, or 36.6 per cent, the intravital diagnosis was based on aspiration biopsy from the lung. By reference to Table IV it may be seen that in the years 1935 to July 1, 1939, aspiration biopsy accounted for 51.6 per cent of all the cases regarded as histologically proved.

TABLE IV

ASPIRATION BIOPSIES VS. BRONCHOSCOPIES (1935 TO 1939)

| | ASPIRATION BIOPSY | BRONCHOSCOPY | OTHER METHODS OR PROVED ONLY BY AUTOPSY | TOTAL |
|------------------|----------------------|--------------|--|-------|
| 1935 | 9 | 10 | 2 | 21 |
| 1936 | 10 | 8 | 2 | 20 |
| 1937 | 15 | 4 | 2 | 21 |
| 1938 | 13 | 9 | 2 | 24 |
| 1939 (to July 1) | 2 | 4 | 3 | 9 |
| Totals | 49 | 35 | 11 | 95 |
| Percentage | 51.6 | 36.8 | 11.6 | 100.0 |

MODES OF APPROACH TO DIAGNOSIS OF CANCER OF THE LUNG

In setting about to confirm histologically a diagnosis of cancer of the lung, certain preliminary examinations are quite essential. First of all, a careful history should be taken, noting as accurately as possible the chronology of symptoms and any etiologic factors that could be considered to have a bearing on the case. The usual complete physical examination is important, particularly with reference to signs of metastases or extensions of the disease. Such points as palpable tracheal deviation, supraclavicular or axillary lymph node metastases, tumefaction of invaded ribs, Horner's syndrome, signs of fluid, cutaneous or distant lymph node metastases (as to the inguinal nodes), signs of bone metastases, and dilated veins on the chest wall, should be particularly observed and noted.

The usual next step is to obtain a posteroanterior erect chest film at 2 M. distance. If on the basis of signs it is possible to localize the

ture in the middle of the area of increased density and in several such cases positive biopsy has been obtained from such "blind" aspirations.

If there is an accessible metastatically involved lymph node, it seems good practice to remove it or at least to obtain an aspiration biopsy from it first, so as to prove the existence of cancer; but it is often difficult for the pathologist to state conclusively whether cancer so identified is of lung origin. If there is a bone lesion, apparently of metastatic origin, or a rib lesion, apparently a direct extension of the lung tumor, an aspiration biopsy of the affected portion of the bone may yield a diagnosis of cancer. Here again it is not entirely satisfactory to rely upon such evidence for proof of primary lung cancer. Since it has been shown that inflammatory pleural effusions may yield clumps of pleural mesothelial cells closely simulating cancer, it is obviously unwise to rely on a diagnosis based, as far as histologic evidence is concerned, solely on the apparent finding of cancer cells in pleural fluid.

As far as proof of primary lung origin is concerned, the same criteria must be applied in large measure to cases with bronchoscopic biopsies as to those with aspiration biopsies, since it is quite possible (and we have observed this in more than one instance) for metastatic lung tumors to erode the bronchial wall. For practical purposes we may decide that a given tumor is primary in the lung if the biopsy is obtained from the lung or bronchus and if there is no evidence of the previous or present existence of a primary tumor elsewhere that would be capable of causing a lung metastasis. However, for absolute proof of primary lung origin, we must demand an unqualified demonstration of that fact both grossly and microscopically by an experienced tumor pathologist at autopsy.

THE TECHNIQUE OF ASPIRATION BIOPSY

Since fear of air embolism (see below) has led to an abandonment whenever possible of the performance of aspiration biopsy of the lung with the patient sitting up, it is now routine practice to localize the tumor fluoroscopically with the patient fully recumbent, in prone, supine, lateral, and oblique positions, and to mark the site of puncture with the patient in the same position that he will be in during the puncture. In the case of small tumors it may be necessary to use fluoroscopic guidance in the course of the aspiration procedure. To this end a biplane fluoroscope of special design would be of great aid. Such a fluoroscope should have no encumbrances about the patient, as is true of the present standard biplane fluoroscopes. The horizontal tube should be 3 to 4 feet away from the patient, and the tube for the vertical beam should be under the floor or at least on the floor so that it will be sufficiently far away to do away largely with distortion. We have not had the advantage of such specially made biplane apparatus, of which there are only a few in existence. When we were doing

the bronchoscopist's notations as to the site of distortion of a bronchus, or the finding of pus or blood that came from a particular branch of the bronchial tree, together with a reconsideration of the chest film, with special reference to how much of the shadow may represent tumor and how much may be caused by atelectatic and inflammatory changes peripheral to the tumor. At this stage lipiodol injection may be very helpful, if it has not already been done. The contour of shadows in well-made lipiodol films, demonstrating bronchial blockage, may be of great service in indicating a likely site for lung puncture. We have not thought it necessary to produce a pneumothorax, in general, and in fact it seems to us more probable that a pneumothorax would in many cases obscure the relations and make it more difficult to localize the tumor.

The old roentgenologic riddle of aneurysm versus mediastinal tumor has caused us much difficulty in several instances. The interpretation of expansion of a mass by fluoroscopy or kymography, together with the aids of tomography and Robb's method of arteriography, all may be called upon in some instances, with, nevertheless, equivocal findings. The double-tube method of fluoroscopic localization, apparently so fool-proof for foreign bodies, would seem to be too hazardous for use for lung aspiration about the hilar fields, involving, as it does, the visualization of a double image of everything in the field, including the needle and the aorta. It has been proved possible in our experience to go into the hilar field under fluoroscopic guidance, in one case passing the needle within 1 or 2 cm. of the left auricle and obtaining a positive biopsy without perceptible harm to the patient. We certainly, however, do not recommend such a procedure routinely, nor would we undertake it save in exceptionally favorable circumstances.

When there are signs of lung abscess the question always arises whether it is safe to do an aspiration biopsy, for fear of spreading infection along the puncture tract. We have successfully performed aspiration biopsy of both cancerous and noncancerous abscesses of the lung in several instances, without, so far as we have been aware, causing any complication. We have never observed empyema following aspiration biopsy. Neither have we ever seen a growth of tumor along the needle tract.

There are certain cases in which it is impossible to determine an optimum site for puncture. The shadow of increased density in the lung field may be large and ill defined and it may be impossible with the aid of lipiodol to judge whether the tumor is likely to be found permeating the entire area of increased density; whereas, if one assumed that the tumor were confined mainly to the medial zone of the area, it would lie in an area too close to heart or aorta or hilar or mediastinal structures to be aspirated safely. In such cases one is justified in selecting arbitrarily what is deemed to be a safe site for punc-

The apparatus for aspiration biopsy is as follows:

1. A 20 c.c. record syringe with smooth action and good fit so that a partial vacuum can be obtained and maintained when the piston is drawn back and the mouth of the syringe is plugged.
2. One or more 18 gauge needles of 10 cm. and 15 cm. lengths; occasionally a 20 cm. needle may be required; the needles should have short bevels.
3. A sharp bistoury.
4. Six clean sterile glass slides.
5. A small curette or scraper for picking tissue particles and adherent clots from the inside of the syringe.

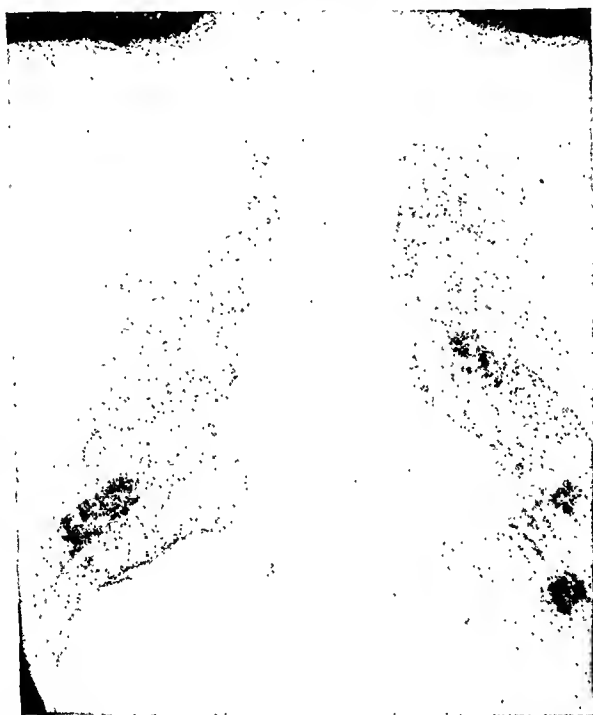


Fig. 2.—Carcinoma of lung, easily accessible by needle puncture, but with negative bronchoscopic findings (see Fig. 1).

6. A hypodermic syringe with needles about 2 inches long so that anesthesia can be carried down to intercostal tissues and pleura.
7. Small glass for holding novocain solution.
8. Sterile test tubes for fluid, blood, pus, or clot.
9. Sterile towels.
10. Sterile gloves.

Aspiration Procedure.—One-half hour before the aspiration the patient receives a hypodermic injection of $\frac{1}{6}$ gr. of morphine sulfate.

The site of election for the puncture having previously been marked with the patient in the same position as that in which he is to be

aspirations with the patient in the erect posture, sitting on a revolving stool, we obtained a biplane examination by very cautious rotation of the patient on the stool after the needle had been inserted as best we could with the guidance of fluoroscopy in one plane. If the straight posteroanterior and the straight lateral views both demonstrate the point of the needle to lie opposite the center of the tumor, the point of the needle must be actually in the center of the tumor.

However, with a patient recumbent, we do not dare risk moving or rotating his body while a needle is in it. That is where a biplane fluoroscope free of encumbering rods and supports for screens would be of



Fig. 1.—Section of clot obtained by aspiration biopsy from tumor shown in Fig. 2. The immediate smear was also quite diagnostic.

great help. Since the abandonment of the erect posture and the performance of all lung aspirations with the patient recumbent or in slight Trendelenburg position, we have had to rely on straight posteroanterior fluoroscopy, plus previous measurement of the depth of the center of the tumor from the skin at the site of the puncture. If the tumor is of more than 5 cm. diameter, it can usually be sufficiently well localized by marking the chest with or without the aid of calipers while the patient is recumbent in the same position that he will be in during the aspiration, measuring both the puncture axis and the depth at a plane exactly 90 degrees to that axis.

with the other hand the piston is pulled out firmly and steadily so that the strongest possible suction is applied. Maintaining this suction is one of the essentials in drawing tissue up into the bore of the needle. While this powerful suction is maintained, the syringe and needle are slowly rotated several times without any deviation from the puncture axis and at the same time the whole syringe-needle system is carefully pulled out and is thrust back in for a very short distance, not over 0.5 to 1 cm. Violent jabbing back and forth to make a pin cushion of a tumor is totally unnecessary and is reprehensible. In the course of this procedure of rotating and moving the needle slightly back and forth, it will usually be found that some of the vacuum has been lost. This is discovered when the piston is slowly allowed, while constantly held, to drift back so as to release the suction, when it will be found, as a rule, that there is an air space of one to two inches beyond the piston, so that it could not be completely let down without actually pushing it down and thus forcing air into the lung. In view of the possibility of air embolism one must carefully avoid forcing any air into the lung, especially not allowing the piston to slip from one's grasp and plunge back into the syringe, an accident which would inject tumor particles and air into the lung.

Upon thus finding a partial loss of vacuum, it is recommended strongly that the syringe be detached and the piston pushed down so as to expel this air. Incidentally, if the syringe at this time contains any blood or fluid, this material should be squirted down to the bottom of a vertically held sterile test tube. In the meantime the gloved thumb of the left hand should have been quickly used to stopper the needle hub as soon as the syringe was detached so as to avoid suction of air through the needle by the patient's inspirations. The syringe, having had its piston completely pushed down again, is reattached to the needle and suction is renewed. This renewal of suction, it is believed, is important and in some cases may be repeated three or four times in order to make more certain of drawing tissue up into the bore of the needle. Then the piston is finally slowly let down to where the pressure condition with the syringe just allows the piston to come to rest, and the needle with the syringe attached is withdrawn from the patient's chest.

COLLECTION OF MATERIAL OBTAINED BY ASPIRATION

This is a part of the procedure that must be carried out meticulously. It must be borne in mind that a fragment invisible to the naked eye may be the telltale fragment under the microscope, especially in cases of punctures that are made in tough resistant tumors from which very little tissue is obtained.

Holding the point of the needle over the center of one of the slides, the stylet is passed slowly through the needle from hub towards point forcing out onto the slide any tissue lying within the needle. Adherent bits of tissue seen at the end of the stylet should be carefully teased

for the aspiration, and preferably marked well outside of the puncture field, so that the imaginary intersection of two lines at right angles indicates the site of the puncture, the area is shaved, if necessary, and prepared by two paintings of iodine, followed by two applications of alcohol to the central part of the area. With 1 per cent novocain, a skin wheal is raised at the site of puncture and gradually novocain is introduced through this wheal to the intercostal space and down approximately to parietal pleura. By this time the skin is thoroughly anesthetized at the wheal, and a tiny incision is made in it with the sharp bistoury, care being taken to sever the bottom elastic layers of the skin so that there will be no skin drag on the needle. The 18 gauge needle is then attached to the record syringe and slowly inserted along the predetermined axis of puncture. Usually the needle is steadily but cautiously advanced along this axis until its point is presumably at the predetermined site in the tumor. Along the way a great part of the caution consists in carefully feeling the type of resistance encountered.

Some carcinomas of the lung will be found almost leathery in resistance to the needle; others have no appreciable difference in resistance from that of normal lung tissue. If a cyst or abscess cavity is encountered, the wall may be resistant and then, as the needle slowly advances, a sudden loss of resistance will be noted as the needle enters the cavity.

There is no need for applying suction until the needle point has reached the desired spot. If the tumor is small so that fluoroscopic guidance is being used to make more certain that the needle reaches the center of the tumor, one prepares to detach the syringe in order to permit the fluoroscopic film to be brought closer to the patient, to within about 2 or 3 inches of the needle hub.

Before detaching the syringe, slight suction is applied in order to make sure that the needle point is not in a vessel or a bronchus. If blood or air is aspirated, the needle is either advanced or withdrawn a little way, until blood or air, as the case may be, no longer enters the syringe on suction. Then, the position of the needle point is checked in the vertical plane by fluoroscopy. Without a biplane fluoroscope or a horizontal x-ray tube with a portable screen the depth of the needle cannot be checked and must have been predetermined by measurements.

If the needle is not in the predetermined puncture axis and thus its point is shown to be to one side of the tumor, the needle must be withdrawn far enough so that without use of any tearing force within the lung its direction can be properly changed and it can be advanced again until it is within the tumor.

When one is satisfied that the needle is within the tumor, one hand grips the barrel of the syringe firmly, holding it absolutely steady, while

less than 18 gauge that might safely be inserted in the depths of the lung without fear of breakage, and with even less danger of trauma to lung tissue.

Dangers of Needle Puncture of the Lung.—In our series of over 230 lung punctures for biopsy we have had very few troublesome sequelae. The most serious accidents were two cases believed to be examples of air embolism. In both cases, while the needle was in the patient, who was sitting up, there was sudden collapse, with tonic and clonic spasms and unconsciousness. Upon recovery of consciousness in about twenty-four hours there were various palsies which rather rapidly decreased in extent and severity so that within three weeks or thereabouts the patients were able to walk, still showing some residual motor impairment. It seemed possible, according to the neurologist, Dr. George H. Hyslop, to exclude intracranial hemorrhage and thrombosis, and he believed the evidence indicated cerebral embolism. Because of the rate and degree of improvement shown and the fact that the accidents occurred in the course of lung aspiration, it is our belief that the emboli were of air rather than solid material. We did not listen over the hearts of these patients for sounds of air bubbles nor did we examine the retinal arteries for air bubbles.

In the belief that a recumbent posture would lessen the damage of air bubbles ascending to the brain, we have done all aspirations in the past year with the patient lying flat, and during the past year no cerebral accidents have occurred.

Slight expectoration of blood may occur for twenty-four to forty-eight hours following an aspiration, but no gross hemorrhage has been encountered. The development of empyema or lung abscess has not been seen, nor has a growth of tumor along the needle tract been found in any case.

Examination of Sputum for Tumor Cells.—In two cases in a recently reported group of 175 cases of bronchiogenic carcinoma the patients happened to save gross pieces of tissue which they had expectorated. These pieces permitted sectioning in the routine manner and gave positive diagnoses. It is our routine prior to bronchoscopy to examine sputum for three successive days for tubercle bacilli and tumor cells. With the exception of the two cases just mentioned, there has been no case in which the examination of the sputum has revealed tumor cells. We have not attempted, however, to develop any special concentration or other technique for this examination. In view of the fact that these two cases yielded macroscopic pieces of positive tissue, it seems quite likely that a special effort to search the sputum day by day might yield positive diagnoses more often, and the effort seems worthy of trial, particularly for cases in which bronchoscopy, aspiration biopsy, or thoracotomy would be difficult.

off and deposited on the slide. Then the syringe may be attached and air blown with a quick thrust through the needle held over the slide, as this procedure may bring down another drop or two of fluid, or tissue fragments.

If within the syringe there is seen a fragment of tissue, it may be fished out with the eurette and deposited on a slide. Another clean slide is placed on top of the one on which the tissue has been deposited and with very firm pressure the two slides are squeezed together and slid along on each other for a short distance and then snapped apart. I prefer this method to drawing one slide or its end along the other, as might be done for blood smears, because it avoids dragging tissue to the ends of the slides, where it may be lost in the staining process. If the syringe, as is often the case, contains 1 or 2 c.c. of blood clot, this should all be carefully saved in a test tube, without crushing, so that it may be prepared in the laboratory for imbedding in a paraffin block and regular sectioning. Even the end of the piston should be carefully searched for tissue fragments and the bits of clot often found adhering to it.

The slides and the tube containing the clot are sent immediately to the laboratory. A report can be obtained on the slides in about ten minutes or less. Thus, if the immediate smear is positive, one may have a diagnosis within one-half hour or less from the time the puncture is begun. If the smear is negative or if its interpretation is difficult, it may be necessary to wait two or three days for the clot to be sectioned and reported. Oftentimes the clot gives very definite information, even as to histologic type. (It may be of interest in this connection to mention a case of atypically located substernal goiter, accessible to aspiration only from the posterior chest wall, in which the sectioned clot showed typical thyroid alveoli containing colloid.)

The details of the laboratory technique of fixing and staining the smears have been described by Martin and Ellis and need not be repeated here.

Caliber of the Aspirating Needle.—An 18 gauge steel needle is about as thin as one would care to risk using for deep-lung aspiration. Needles of 17 gauge are just enough thicker to give the impression of being too large and offering too much chance of trauma to vessels and bronchi. Were it possible to use a needle of even smaller bore than 18 gauge without risk of having it break, it should be possible to secure tissue almost as well. It is true that, when an aspiration biopsy done with an 18 gauge needle is positive, one usually has many times the amount of tissue that is needed. On this premise aspiration biopsies of subcutaneous tumors have been tried with ordinary 26 gauge hypodermic needles, and have been successful. Perhaps some of the newer alloys, such as are used for dentures, could be used for making needles of

RESECTION OF THE LUNG*

EDWARD D. CHURCHILL, M.D., BOSTON, MASS.

(From the Harvard Medical School and the Surgical Services of the Massachusetts General Hospital)

IN PAYING tribute to the memory of Edward Starr Judd by this lecture, I have selected the subject of pulmonary resection and shall present it with emphasis on the problems of operative surgery. There is no more fitting place to do this than in a lecture by a surgeon in honor of a master surgeon. Although Judd was endowed to a remarkable degree with the many other qualities that must be joined to make up the complete master surgeon, no single quality or achievement surpassed his skill and judgment in operative surgery; in this field he was pre-eminent.

Resection of a diseased organ is admittedly a crude and primitive form of therapy when compared with subtleties of modern surgery, such as removing a tiny adenoma of a parathyroid gland to prevent the recurrence of stones in the kidney or interrupting the sympathetic chain in order to preserve a limb by increasing its blood supply. The principles involved in the case of the lung are so simple and the attack so straightforward that practically the only argument lies in balancing the operative risk against the natural hazards and disabilities of the disease for which it is proposed. We may contrast lobectomy for bronchiectasis, where the question is not should it be done but can it be done, with gastrojejunostomy for duodenal ulcer where the pertinent question is not can it be done but should it be done.

Pulmonary resection is carried out as the removal of one entire lung (total pneumonectomy), the removal of one or more lobes of one lung (lobectomy, single or multiple, unilateral), the removal of lobes from both lungs (lobectomy, bilateral), the excision of a bronchovascular segment from one or more lobes (segmental pneumonectomy), or the resection *en bloc* of a portion of a lobe (partial lobectomy) or lobes (partial pneumonectomy). These operations may be one-stage, two-stage or multiple-stage procedures.

GENERAL CONSIDERATIONS

As a rule, in pulmonary surgery a two-stage procedure is carried out with the purpose of obliterating the whole or a portion of the fre-

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SUMMARY AND CONCLUSIONS

1. Histologic proof of cancer should be a prerequisite to radical surgical or radiological treatment of cancer of the lung.

2. In a considerable proportion of cases of lung cancer bronchoscopy will not yield a positive microscopic diagnosis.

3. In the 175 cases of cancer of the lung treated at Memorial Hospital from Jan. 1, 1920, to July 1, 1939, the intravital histologic diagnosis was made on material obtained by lung puncture in 64 cases, or 36.6 per cent; and since January, 1935, aspiration biopsy was called on to furnish the histologic material in 49 of 95 cases, or 51.6 per cent.

4. The technique of surveying a case suspected of having cancer of the lung and the technique of aspiration biopsy of the lung are given in detail.

5. The hazards of aspiration biopsy are discussed. In the Memorial Hospital series of 230 lung aspirations there has been observed no case of empyema, lung abscess, or growth of tumor along the puncture tract. Two cases believed to be examples of air embolism resulting from lung puncture have been seen. On the theory that air bubbles introduced into the pulmonary venous system and thus via the left heart into the systemic circulation tend to ascend, because of the lighter specific gravity of air as compared with blood, it is recommended that all lung punctures be done with the patient lying flat or in slight Trendelenburg position, so as to minimize the danger of air bubbles going cephalad.

6. It is advisable to use needles of the smallest caliber consistent with minimal danger of breakage, since successful aspirations can be obtained from subcutaneous tumors even with hypodermic needles if the proper technique is employed.

7. Development of techniques of searching sputum for tumor cells is worthy of trial.

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Anesthesia.—There are certain general principles that govern both the choice of the anesthetic agent and the method of administration. Differential pressure is essential if the goal of a painstaking operation of precision with careful hemostasis is to be achieved. With present techniques adequate control of differential pressure presupposes an inhalation anesthetic, the alternative being a return to the elaborate and cumbersome methodics of the differential pressure cabinets of Sauerbruch, Robinson, and Willy Meyer. Inhalation anesthesia can be administered with control of differential pressure by using a tightly fitting face mask. Intratracheal intubation in addition to a tightly fitting mask is a more certain method and avoids inflation of the stomach.

A second important principle centers on keeping the airway clear of bronchial secretions and purulent exudate. Even though postural drainage or bronchoscopic aspiration is carried out immediately before the operation, mobilization of an infected lobe or lung expresses retained secretions into the primary bronchi and trachea. It is important to provide for the intermittent aspiration of this material during the course of the operation. Attempts have been made to blockade the infected area of lung by balloon-tipped catheters or intrabronchial tamponade, but these complicated methods will not be found necessary if efficient aspiration is carried out. This can only be done if an intratracheal tube is employed and preferably one inserted directly into the larynx rather than through the nasal route and of a cross-sectional area approximately one-half that of the trachea.

The third important principle conditions the choice of the anesthetic agent itself, as it is the rigid avoidance of anoxia during the operation and subsequently. Excluding chloroform, there are only two anesthetic agents in common use that can be administered by inhalation with sufficient concentration of oxygen to fulfill this essential requirement: cyclopropane and ether vapor. Not only because of the explosion hazard of cyclopropane but because of its apparent selective toxic effect on the heart, it has been our custom to employ ether.

At the present time, therefore, unless unusual indications are present, pulmonary resection is carried out under general inhalation anesthesia with an ether vapor oxygen mixture administered through an intratracheal tube with a closed system that permits the maintenance of differential pressure and affords ready access for aspiration of the tracheobronchial tree.

Incisions.—The merit of any surgical incision lies in affording access to the region of dissection with a minimal degree of damage to normal structures. The exposure must be adequate to permit dissection of important structures under direct vision and adaptable to any variations in pathology that may be encountered. A needlessly large

pleural space at the first operation in order to prevent or limit a subsequent pleural infection and avoid the complications of a collapse of the remaining part of the lung by a pyopneumothorax. There are other reasons, however, for dividing these operations into stages. Dense and vascular adhesions or other difficulties may make it advisable to perform a total pneumonectomy by removing the lower lobe at one operation and the remaining lobe or lobes at a subsequent date (total pneumonectomy by lobar stages). The very dense adhesions of active infection may force the operator to abandon entirely the project of immediate resection even of a single lobe and to resume the dissection at a second stage. It must be pointed out, however, that such a retreat, once the mobilization of the lung is well on its way, may be as hazardous as pushing the job to its conclusion, as the stage is set for pleural infection from divided adhesions and a pneumonic flare-up spreading from traumatized infected lung.

Ligation of the lobar division of the pulmonary artery was suggested by Sauerbruch¹ as a first-stage procedure in lobectomy. Rienhoff² recommends ligation of the stem branch of the pulmonary artery as well as the main bronchus as a first-stage operation in total pneumonectomy.

Canterey lobectomy or pneumonectomy (Graham) and exteriorization lobectomy (Whittemore) marked evolutionary stages in pulmonary resection and must be classified as partial or, at the best, subtotal procedures. Both operations now find a very limited sphere of usefulness or have been completely abandoned.

Removal of a lobe or lung has been accomplished by placing an elastic tourniquet around the hilum (Sauerbruch) or by the use of mass constricting ligatures (Alexander), waiting for the devitalized tissue to sequester or removing it at a later operation. These methods were cumbersome and invited dangers of both hemorrhage and infection. They belong to the historic aspects of pulmonary surgery.

At the present time pulmonary resection is approached in a direct manner in accordance with surgical principles established for other organs of the body. The hazards of hemorrhage, primary or secondary, have been brought under satisfactory control. The complications of infection have been lessened but still remain formidable and a source of constant apprehension. Only a beginning has been made toward insuring a balanced equilibrium of the cardiorespiratory functions during and after surgical intervention. Even the most meticulous techniques seriously encroach upon the wide margin of safety with which the body safeguards its important physiologic mechanisms, and, when this is greatly narrowed by age or grave functional disability, radical pulmonary surgery is as yet impossible.

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opening into the thorax is to be avoided because of the crippling of the mechanism of respiration it entails. Respiratory movements of the thoracic wall are undoubtedly a factor in promoting re-expansion of the underlying segments of lung in the postoperative period. Unnecessary damage to the latissimus dorsi and other important muscles that take part in coughing makes it increasingly difficult to maintain post-operative bronchial drainage.

Whether an anterior or posterior approach is employed, whether a rib is resected or the incision carried through an intercostal space, whether the incision is placed high or low, are details that each surgeon must settle for himself, and concerning which we may never expect unanimity of opinion. Personally, for a lower lobe lobectomy I prefer a posterior approach through the periosteal bed of the eighth rib. For a total pneumonectomy I prefer a posterolateral approach at the level of the fifth, sixth, or seventh rib, choosing a high approach if difficulty is anticipated with apical adhesions and a lower approach if basal adhesions are more likely. To gain access to the upper lobe either a posterolateral or anterolateral incision is employed. An anterolateral incision gives direct access to the middle lobe on the right or the lingula segment on the left.

Pleural Adhesions.—It is generally believed that a partial resection of one lung (lobectomy, segmental pneumonectomy, etc.) carries a lower incidence of complications and a lower mortality rate if there exists at the time of operation a complete symphysis of parietal and visceral pleura. Probably this is true if the resection is being performed for suppurative lesions in which empyema is an inevitable sequel. Obliteration of the pleural space over the surface of the lung that is to remain goes a long way toward insuring its integrity and limits the extent of the infection.

In the case of noninfected lesions in which pleural contamination is minimal or nonexistent, and in total pneumonectomy, pleural symphysis is undesirable. Pleural adhesions that are dense and vascular in themselves may add hazards to the operation that more than counterbalance the advantages of an obliterated pleural space even in suppurative disease.

On the assumption that pleural symphysis is a decided advantage, methods of artificially producing a fibrinous pleuritis have been studied in the experimental laboratory and have received clinical trial. Open thoracotomy as the first stage of lobectomy for bronchiectasis was at one time recommended by Alexander.³ I⁴ also employed it in selected cases. Pre-existing adhesions around the lobe to be resected were severed and the pulmonary ligament divided. Nonadherent areas of the parietal pleura were vigorously scrubbed with dry gauze and the chest closed. Alexander proceeded with the second stage within

approximately two weeks, while I recommended a delay of three months or longer to allow the acute reaction completely to subside.

There are several disadvantages to this method, not the least of which is twice subjecting a patient to the hazards of an anesthetic and thoracotomy. Pleural infection was occasionally encountered after the first stage. Also, not infrequently the procedure failed to produce the desired adhesions. Use of this method has almost completely been abandoned and it is recommended only if some special reason exists for anticipating difficulty in obtaining re-expansion of the remaining lobe; for example, in the case of a patient who has received prolonged artificial pneumothorax with resulting fibrosis of a non-adherent visceral pleura.

Bethune⁵ devised a method of producing pleural symphysis known as "poudrage." An artificial pneumothorax is induced and talc or other mildly irritating substance is dusted on the pleural surface under guidance of the thoracoscope. Clinical reports are still too fragmentary to yield an evaluation of poudrage.

During recent years attention has been diverted from the artificial production of pleural symphysis toward active measures for encouraging early re-expansion of the remaining nonadherent lobe. The problems involved are discussed under a separate heading.

When adhesions already obliterate the pleural space, they are usually readily dealt with, but may in certain instances present a formidable barrier to surgical dissection. This is particularly true in the chronic lung abscess group with long standing and still active pneumonitis. Nevertheless, I join with Roberts and Nelson⁶ in doubting "that there are any adhesions which cannot be overcome by careful dissection." Adhesions that found their origin in an episode of infection that is quiescent at the time of operation offer little difficulty. They are relatively avascular and may easily be divided by sharp dissection. Cutting under direct vision is always preferable to blunt dissection or manual separation as the fragile surface of the lung can be damaged by the use of any force. This is particularly true if compensatory emphysema is present. Transillumination of adhesions aids in the recognition of the margin of the lung and will disclose large blood vessels before they are divided.

Adhesions are best divided as close to the visceral pleura as possible. This prevents the retraction of bleeding vessels into the chest wall in what may be regions of difficult access. Bleeding from the pulmonary side of an adhesion is rarely troublesome unless the lung itself is badly torn by forceful maneuvers. Hemorrhage from the parietal side may be profuse and difficult to control. Absolute hemostasis at the end of the operation is imperative as the negative pressure re-established immediately after the incision is closed encourages postoperative

bleeding. This may be life-endangering or add to the complications of postoperative management by plugging the drainage tubes with blood clot. A massive postoperative hemothorax may require surgical evacuation.

The Interlobar Fissures.—The operation of lobectomy is not infrequently made difficult by anatomically incomplete interlobar fissures or by the obliteration of normal fissures by adhesions of inflammatory origin. The problem presented by abscesses traversing the plane of the fissures is discussed under a separate heading.

Incomplete fissures offering technical difficulty most often will be found between the dorsal segments of the lower lobes and the corresponding upper lobes. It is essential that all adjacent interlobar fissures be artificially completed to the hilum before a tourniquet is placed about the lobe. This is accomplished by the division between clamps of the pulmonary tissue in the projected plane of the fissure and the placement of hemostatic sutures. The peripheral portion of an incomplete fissure may be developed by painstaking sharp dissection, reserving the use of clamps until the vascular anastomoses that occur in the hilar region are encountered.

The fissure between the middle lobe and the right upper lobe is notorious for being incomplete or totally absent, particularly in the anterior and mediastinal region. It has been found advisable under such conditions to sacrifice a normal middle lobe with a diseased right upper lobe rather than undertake the development of this fissure. Segmental deflation as described under segmental pneumonectomy has been used to advantage to display the plane between upper and middle lobes in the completion of this fissure, the occluding clamp being placed on the middle lobe bronchus.

The development of fissures that are obliterated with inflammatory adhesions offers technical difficulties that range from the simple to the frankly impossible. If one of the lobes is normal, however, painstaking dissection will permit their separation. A normal lobe (excepting occasionally the right middle lobe) should never be sacrificed solely on the grounds of an incomplete or obliterated fissure.

Drainage.—Provision is made for drainage of the pleural cavity in every case in which a portion of a lung has been resected. In non-suppurative cases or when contamination is minimal, an intercostal catheter is used and removed at the end of forty-eight hours. When tourniquet lobectomy has been performed, a longer drainage period will usually be advisable. I have come to this point of view only with reluctance as I am a firm believer in the general principle of the primary closure of wounds in uninfected surgical fields.

When virulent anaerobic infection is present, the need for more ample drainage is anticipated by rib resection and the placement of

a large tube. Rib resection drainage is also established primarily when pleural symphysis insures a small localized empyema cavity. To state the matter simply, the type of drainage is employed that would be indicated if the empyema already existed, but is carried out in anticipation of its actual occurrence.

After total pneumonectomy by individual ligation of vessels and suture of the bronchus, drainage is omitted if contamination has been minimal. Primary healing of the pleural cavity by the formation of a sterile fibrothorax may eliminate the necessity of a subsequent thoracoplasty. After total pneumonectomy with the tourniquet technique for suppurative lesions, drainage is provided and subsequent thoracoplasty accepted.

Just as recent developments in chemotherapy are modifying the occurrence and course of postpneumonic infections of the pleural cavity, so may the situation be changed relative to postoperative infections. Clinical tests are being made both with the local application of chemotherapeutic drugs to the pleural space and with the preoperative and postoperative establishment of an effective concentration in the blood stream.

Re-expansion of Remaining Lobe.—Following lobectomy, the concern of the immediate postoperative period centers on the re-expansion of the remaining lobe. Operative sequelae that jeopardize the integrity of the remaining lobe are varied in type and origin and it is impossible to abstract from the literature any coherent account of their nature or even of their incidence. It may also be noted that there are no data on record to indicate an increased morbidity when lobectomy is performed in the presence of a free pleural space, although this is commonly assumed to be the case.

Complications involving the remaining lobe or lobes on the operated side cannot be discussed at length, but will be briefly outlined because there is a tendency to hold too limited a view as to their origin and nature. My point of view, in general, coincides with that expressed by Edwards¹⁹ that the lesion responsible for collapse is within the lung itself and not in the pleura.

1. *Apical Empyema:* Failure of the upper lobe to regain its integrity after a lower lobe lobectomy is commonly associated with an apical empyema. This is usually considered as the primary disturbance, but in my experience apical empyema is apt to be secondary to intrinsic disease of the underlying lung. If recognized promptly and given adequate drainage, an uncomplicated apical empyema that has become walled off from the basal area is not commonly serious or of lasting import. Postoperative collections of air or serum in the apical region should be aspirated frequently and may escape infection even though a frank empyema exists at the base. When infected, drainage in the axilla will usually be followed by re-expansion of the lobe.

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There is a general impression that resection of an upper lobe presents a more difficult problem of healing than is the case with lower lobe resection. In my experience this has not been the case, as in nine patients surviving upper lobe lobectomy an apical thoracoplasty has been found necessary only in one instance (Fig. 1).

Technical measures designed to promote early expansion of the remaining lobe are under constant scrutiny. Aspiration of residual collections of air and serum has been mentioned. The placement of an anterior intercostal catheter in addition to posterior drainage may be advantageous. Postoperative bronchoscopy is indicated, particularly if there is evidence of occlusion of major bronchi. Complete reinflation

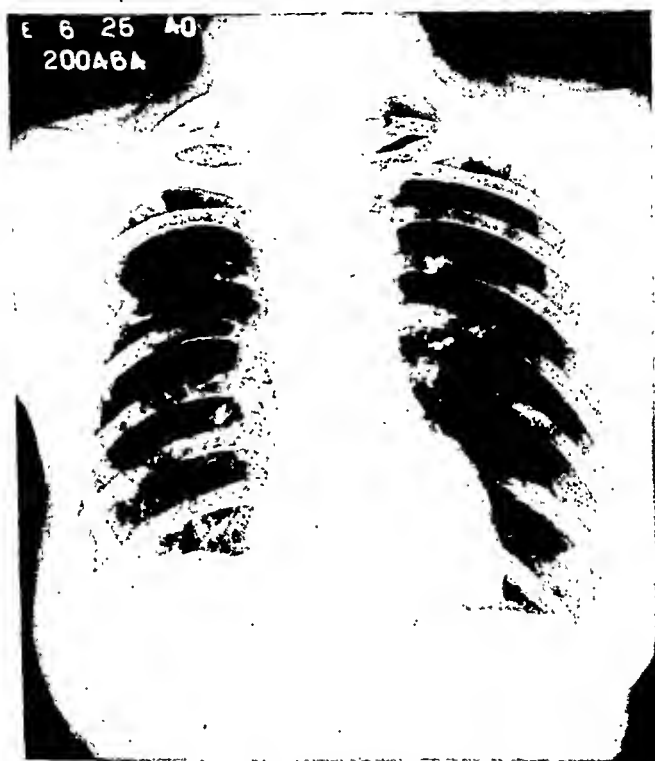


Fig. 1.—Roentgenogram taken eight months after resection of normally inflated right upper and middle lobes for bronchiectasis. Postoperative staphylococcus empyema.

of the lung by positive pressure as the chest is being closed is essential. Postoperative administration of oxygen and helium under positive pressure is recommended on theoretical grounds and is now receiving clinical assay.

Preoperative Artificial Pneumothorax.—It is assumed that there are several advantages to be derived from inducing artificial pneumothorax as a preoperative measure before total pneumonectomy for tumor. These may be listed with brief comments as follows:

2. *Atelectasis and Pneumonitis:* Atelectasis as a concomitant of post-operative pneumonitis and bronchitis may occur with or without gross obstruction to the large bronchi. Under such circumstances the failure of the lobe to re-expand is due to intrinsic factors and the apical empyema is secondary, both in origin and in importance. Drainage of the empyema under such circumstances may bring the lobe into contact with the chest wall by a shift of the mediastinum, with resulting obliteration of the pleural space but with the lobe still in a collapsed state. It is my opinion that intrinsic atelectasis and pneumonitis are commonly the first step in the complications that permanently affect the upper lobe. Minimal degrees occur not infrequently and clear spontaneously aided by breathing exercise.

In an effort to reduce this complication, further attention must be directed toward the preoperative condition of the lung. Belsey⁷ has commented on the advisability of a prolonged interval between the injection of lipiodol and operation. It is our custom to demand six weeks as a minimal interval. Recent episodes of acute respiratory tract infection may pave the way for postoperative sequelae. Particularly important, however, is the existence of foci of bronchiectasis unrecognized by bronchography, or a mild degree of atrophic cylindrical bronchiectasis. Obstruction to major bronchi with resulting atelectasis may arise from inflammatory hyperplasia of hilar lymph nodes.

3. *Suppuration:* I have twice encountered frank suppuration with abscess formation in the upper lobe following lower lobe lobectomy. In both instances the lingula had been resected for extensive involvement. It is probable that this serious and formidable complication arises from operative injury to the lobe, infection centering in residual suture material or residual bronchiectatic foci. Resection of the upper lobe becomes necessary in the end.

4. *Gangrene:* Gangrene of adjacent lobe has been described as a complication of lobectomy but has not been encountered personally. While unrecognized operative injury to the vascular supply is the most likely etiology, the possibility of a retrograde thrombophlebitis is to be considered.

The volume of resected lung as measured in its preoperative state of inflation determines within general limits the readiness with which the residual space will be filled by remaining lung. Other variables, such as flexibility of the mediastinum and elevation of the diaphragm, also play their part. Little difficulty is encountered after the resection of a lobe for the atelectatic type of bronchiectasis as the remaining lobe is "accustomed" to filling the hemithorax. This contrasts with the prolonged healing that may be encountered, for example, after resecting right lower and middle lobes that are air containing and essentially of normal volume. These considerations are of importance in giving an estimate of the period of convalescence and the likelihood of complications.

monectomy is performed for tumor. Before lobectomy and in suppurative lesions of the lung there are few indications for its use.

Needle Aspiration Biopsy.—In the presence of bloody pleural fluid the diagnostic advantages of aspiration with or without subsequent thoracoscopy are obvious. Needle biopsy of the tumor itself to establish a microscopic diagnosis in cases that are clearly inoperable is also permissible. On theoretical grounds it is a highly questionable procedure to traverse the pleural space and normal lung tissue with a needle in order to obtain a biopsy from a tumor that may be operable. In such instances thoracotomy will usually be required to settle the question of operability and any reasonable doubt as to diagnosis may be clarified at that time.

TECHNIQUES OF PULMONARY RESECTION

Before discussing the applicability of different operative techniques in varying pathologic conditions, it is desirable to describe the several methods of pulmonary resection in some detail.

Tourniquet Lobectomy and Pneumonectomy.—While Brunn⁸ deserves the credit for pointing out the advantages of a direct one-stage amputation of a lobe, the ingenious method of dealing with the pedicle originated by Shenstone has contributed enormously toward the ease and safety of the operation. The Shenstone tourniquet, or one of its various modifications, is slipped over a mobilized lobe and grasps the hilar pedicle as a snare. Distal amputation of the lobe is then carried out and the blood vessels and bronchi of the stump are secured with stitch ligatures. Release of the tourniquet then allows a neat closure of the stump by suture of the fringe of lung and visceral pleura. If normal lung tissue is available near the hilar region of the lobe, a pedicle flap outlined as the lobe is being amputated aids in a plastic reinforcement of the closure.

In the case of a total pneumonectomy the entire lung is mobilized and the tourniquet used to grasp the hilum. After amputating the lung, the stump is handled as in a lobectomy.

The advantage of the tourniquet technique lies in the ease with which the hilar stump may be closed without recourse to the crushing action of clamps or the use of mass ligatures. Suggestions that the cord of the tourniquet be left in place as a constricting ligature show a failure to grasp the real significance of the method.

The limitations and disadvantages of this form of treatment of the hilum must be kept clearly in mind. Even though constricting mass ligatures are avoided, the sutures necessary for hemostasis and bronchial closure cannot be placed with precision and of necessity result in devitalization of the contaminated tissues of the stump. Suturing this conglomerate mass of lymph nodes, large blood vessels and contaminated bronchi with chromic catgut has always been a revolting

1. *To Lessen the "Shock" of Opening the Pleural Cavity:* With adequate control of lung inflation by differential pressure and the avoidance of anoxia there is no disturbance of the patient's equilibrium when the chest is opened.

2. *To Stimulate a Defense Mechanism to Infection by Calling Forth a Nonspecific Inflammatory Reaction in the Pleura:* The immunologic problems involved are too complex to warrant discussion of the hypothesis constructed on this basis. One recalls the experimental and clinical evidence for and against peritoneal "vaccination."

3. *To Adjust the Organism to Maintaining Respiratory Function With One Lung:* No definitive data are available to indicate whether pneumothorax really accomplishes this result. Further clinical and experimental evidence is highly desirable.

4. *To Provide a Test of Function of the Lung That Is to Remain:* There is not available at the present time an adequate technique for determining what by analogy with the kidneys may be termed a divided or "split" test of pulmonary function. The nearest approach lies in partially reducing the functional capacity of the lung that is to be removed by an artificial pneumothorax. It is to be borne in mind that a closed pneumothorax only partially reduces the function of the lung that is collapsed.

5. *To Determine the Existence and Site of Pleural Adhesions:* Information that aids in the proper placement of the incision may be gained by pneumothorax. Usually this is obvious from studying the location of the tumor.

6. *To Aid in the X-ray Diagnosis and the Determination of Criteria of Inoperability:* Pneumothorax at times may clarify questions of chest wall or mediastinal invasion or aid in the delineation of mediastinal lymph node involvement.

7. *As a Preliminary to Thoracoscopy:* In a small number of peripherally situated tumors thoracoscopy may provide information of importance, particularly with reference to the presence of pleural seeding. Positive evidence is more important than negative, as pleural implantations may readily be overlooked. In bloody effusions aspiration with air replacement is indicated both as a palliative measure and for further diagnostic studies by x-ray and thoracoscopy if necessary.

There is no evidence at the present time that warrants the use of preoperative pneumothorax when lobectomy, in contrast to total pneumonectomy, is contemplated. A rare exception may be found in its use as a diagnostic measure. Before total pneumonectomy for suppurative lesions, pneumothorax is usually impossible and may be positively dangerous as it invites infection of the pleural space.

It may be concluded that preoperative artificial pneumothorax may be informative and possibly beneficial to the patient before total pneu-

ment (Fig. 2). As this is followed centrally, two other divisions of the pulmonary artery are disclosed that often arise at approximately the same level. One of these runs forward to supply the lingula segment of the upper lobe, and the other courses backward and downward as the artery to the dorsal segment of the lower lobe. The latter artery is usually obscured at its point of origin from the main trunk by a lymph node. Mobilization of the lymph node, particularly if it is hyperplastic, is necessary before the artery can be isolated and a ligature passed around it. Ligation of the arterial supply to the left lower lobe is therefore accomplished by securing *two* vessels, the artery to the basal segment which is readily exposed and the artery to the dorsal segment which requires further dissection. As anatomic studies of the intrahilar region are broadened and multiplied, anomalous arrangements will

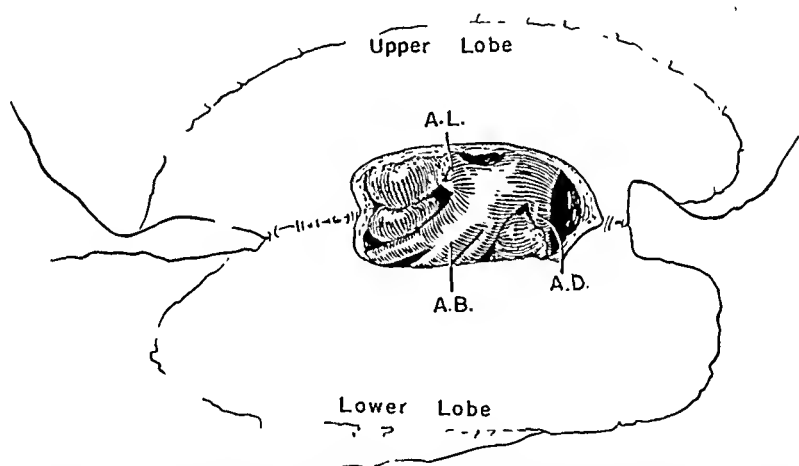


Fig. 2.—Dissection at base of fissure between upper and lower lobes of left lung. A. L., Artery to lingula; A. D., artery to dorsal segment of lower lobe; A. B., artery to basal segments of lower lobe.

undoubtedly be recognized as commonplace. The lingula and dorsal lobe arteries have been observed, for example, to arise in a common trunk. The important safeguard in intrahilar resection of the left lower lobe is to visualize clearly the relations of these two vessels.

The inferior pulmonary vein collects the return flow of blood from the left lower lobe and conveys it to the left auricle. Its main trunk is found at the upper end of the pulmonary ligament by turning the lower lobe forward and dividing the pleura where it is reflected from the lung to the posterior mediastinum (Fig. 3). There are two major tributaries of the inferior pulmonary vein, one from the dorsal segment and the other from the basal segment of the lobe. Usually a third tributary will be disclosed joining these in the extrapericardial and extrapulmonary segments of the inferior pulmonary venous system.

task to the surgeon whose horizon extends to the period of tissue repair. The surprising thing is not that the method is eminently successful but that it works at all. While temporary bronchopleural fistulas almost always appear, they close as the empyema heals. The fact that secondary hemorrhage from the stump has not occurred, at least in my own experience, can only be attributed to the low head of pressure in vessels of the pulmonary circuit.

The plane of amputation with the tourniquet technique as applied to a lower lobe, passes through the origins of the terminal bronchi of the basal segment, and divides the dorsal segment bronchus distal to its first subdivision. In the case of a total pneumonectomy, the plane of amputation passes through the lobar bronchi. While in a few cases section at a higher level can be carried out by this method, individual ligation of the vessels is preferable if the stump is to be appreciably shortened. A short stump invites retraction from the tourniquet or may allow a large vessel to be turned into a bronchus so that endobronchial hemorrhage occurs when the tourniquet is released. Needless to say, control of the stump should never be entrusted to the tourniquet alone. As soon as amputation is started, clamps are used to grasp the bronchi and vessels distal to the tourniquet, and, as sutures replace the clamps, the long ends are used to steady the hilum and prevent retraction from the cord of the tourniquet.

Intrahilar Lobectomy.—If access to the hilar region is blocked by inflammatory reaction, enlarged lymph nodes, or unusually rudimentary fissures, the necessity for tourniquet amputation is conceded. When technically feasible, however, it is preferable to carry out lobectomy by individual ligation of the pulmonary vessels and amputation of the lobar bronchus as an isolated structure. The required dissection opens an unwritten chapter in surgical anatomy, and I shall briefly sketch its problems. While variations will be encountered in the anatomic pattern of the segmental divisions of the pulmonary vessels and bronchi, a general conception of the required techniques is given in the accompanying description and illustrations.

The fact that intrahilar lobectomy is more time consuming than tourniquet lobectomy must be taken into consideration before undertaking this type of operation in poor risk patients. On the other hand, a fair trial of the method gives evidence of an encouraging diminution of the suppurative complications of convalescence and a lessened incidence of temporary bronchial fistulas. Assessment of any influence on the mortality rate must await further experience.

Left Lower Lobe: The terminal divisions of the left pulmonary artery supplying the lower lobe are disclosed at the base of the fissure between lower and upper lobes. Incision of the visceral pleura at the base of the fissure discloses a large artery that supplies the basal seg-

bronchus arises only a few millimeters above the orifice of the bronchus to the dorsal segment. The pulmonary artery is found in the base of the fissure between upper and lower lobes by retraction of the middle

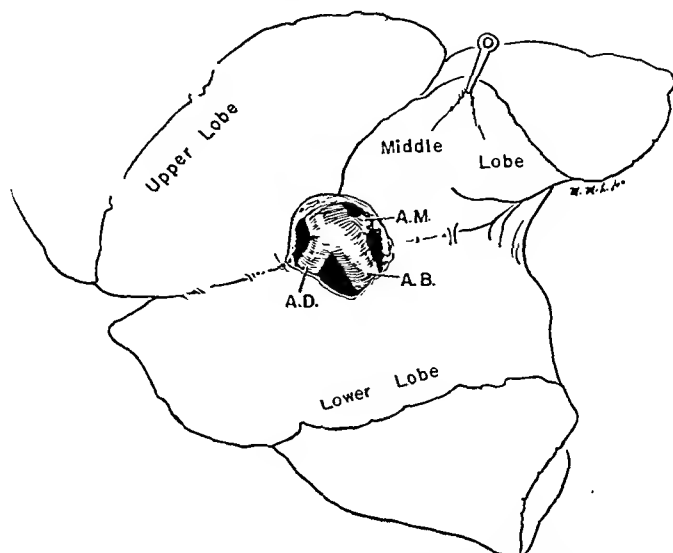


Fig. 5.—Dissection at base of fissure between upper and lower lobes of right lung. Middle lobe carried forward with hook. A. D., Artery to dorsal segment of lower lobe; A. B., artery to basal segments; A. M., anterolateral artery to middle lobe.

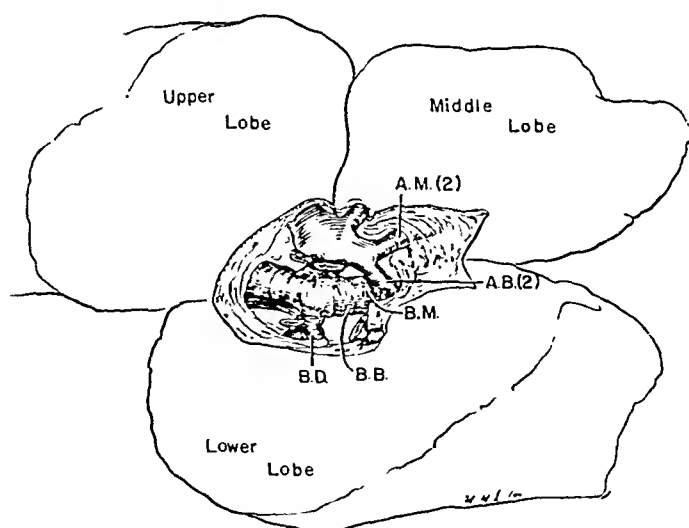


Fig. 6.—Further dissection right hilum. A. M. (2), Artery to medial segment of middle lobe; A. B. (2), artery to mediastinal basal segments of lower lobe; B. M., middle lobe bronchus; B. D., bronchus to dorsal segment; B. B., bronchus to basal segments.

lobe forward and incising the visceral pleura (Fig. 5). The two large terminal divisions of the right pulmonary artery, dorsal and basal, are readily exposed, and a smaller division coursing forward to the middle

Isolation and ligation of the inferior pulmonary vein as a single vessel are possible if care is taken to stay beyond the line of pericardial reflection. Ligation of the three tributaries of the vein is often preferable and is excellent insurance against damage to the pericardium.

After doubly ligating and dividing the vascular supply of the lobe, any fissures that remain incomplete may be developed and the bronchus isolated as a single structure. A Shenstone tourniquet, rather than a clamp, is employed to occlude the bronchus while it is amputated and sutured (Fig. 4). If the pathologic lesion for which the

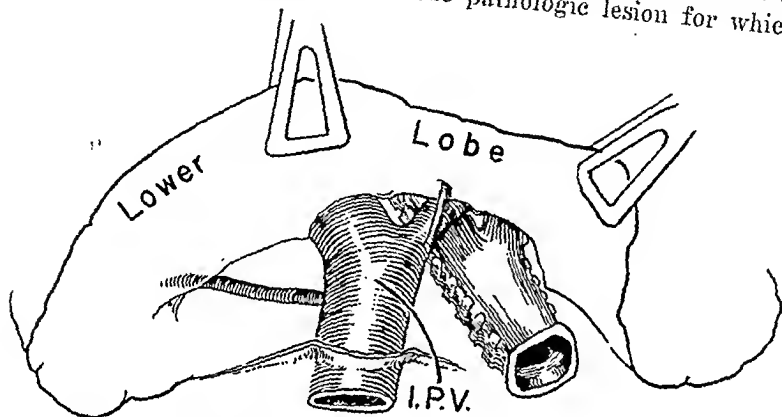


Fig. 3.—Hilar dissection left lower lobe. I. P. V., Inferior pulmonary vein.

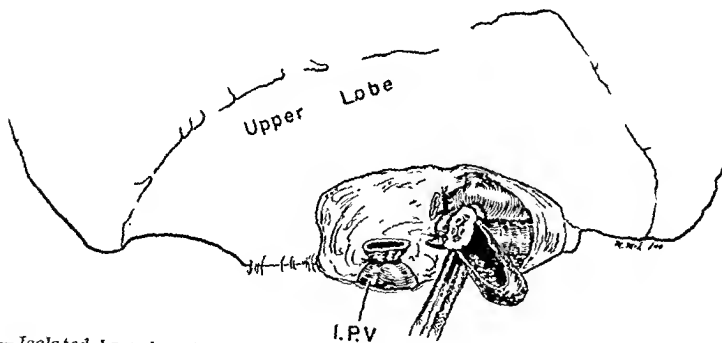


Fig. 4.—Isolated bronchus to left lower lobe grasped by tourniquet. Flap of lung for plastic closure.

resection is being performed permits, a small flap of lung tissue is left attached to the bronchus by a pedicle and used to cover the sutured end. If this is not available, adjacent mediastinal or pulmonary tissue from another lobe is utilized for this purpose. A lobar branch of the bronchial artery may be encountered in close proximity to the posterior aspect of the bronchus and require ligation.

Right Lower Lobe: Resection of the right lower lobe by this method is made somewhat more complicated by the fact that the middle lobe

bronchus arises only a few millimeters above the orifice of the bronchus to the dorsal segment. The pulmonary artery is found in the base of the fissure between upper and lower lobes by retraction of the middle

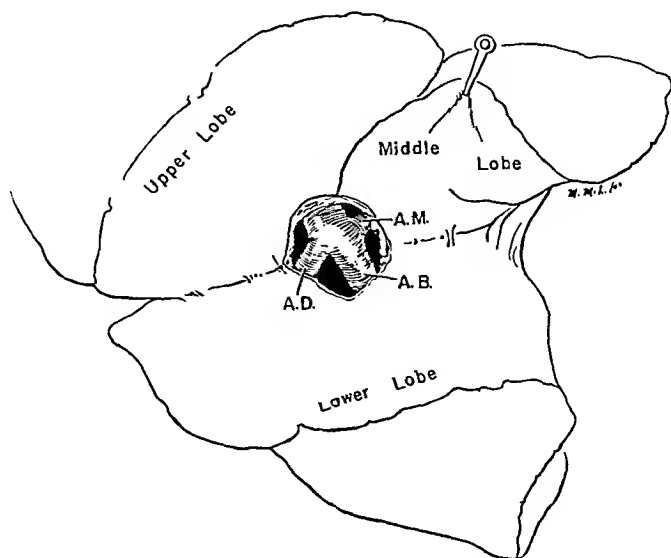


Fig. 5.—Dissection at base of fissure between upper and lower lobes of right lung. Middle lobe carried forward with hook. A. D., Artery to dorsal segment of lower lobe; A. B., artery to basal segments; A. M., anterolateral artery to middle lobe.

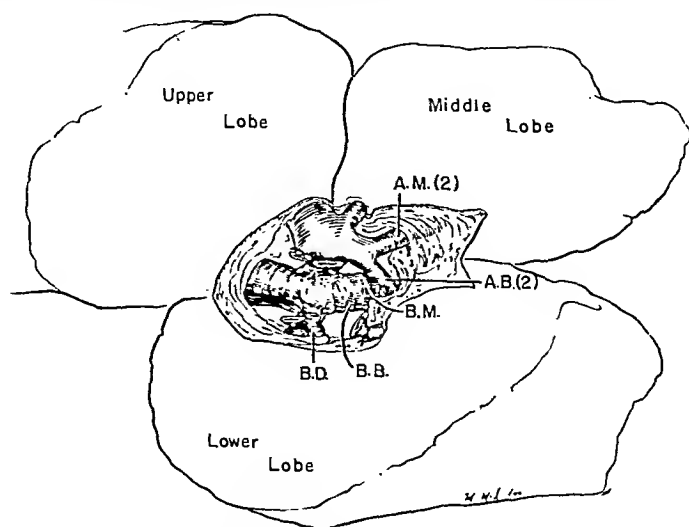


Fig. 6.—Further dissection right hilum. A. M. (2), Artery to medial segment of middle lobe; A. B. (2), artery to mediastinal basal segments of lower lobe; B. M., middle lobe bronchus; B. D., bronchus to dorsal segment; B. B., bronchus to basal segments.

lobe forward and incising the visceral pleura (Fig. 5). The two large terminal divisions of the right pulmonary artery, dorsal and basal, are readily exposed, and a smaller division coursing forward to the middle

lobe can be identified. The dorsal and basal segmental arteries are divided between ligatures and as their ends retract two further divisions will be exposed that had remained concealed (Fig. 6). The more central one of these is a second artery to the middle lobe and is to be preserved. The other passes downward to supply the mediastinal basal segment and is divided between ligatures.

The inferior pulmonary vein is exposed as in a left lower lobe lobectomy and handled in a corresponding manner.

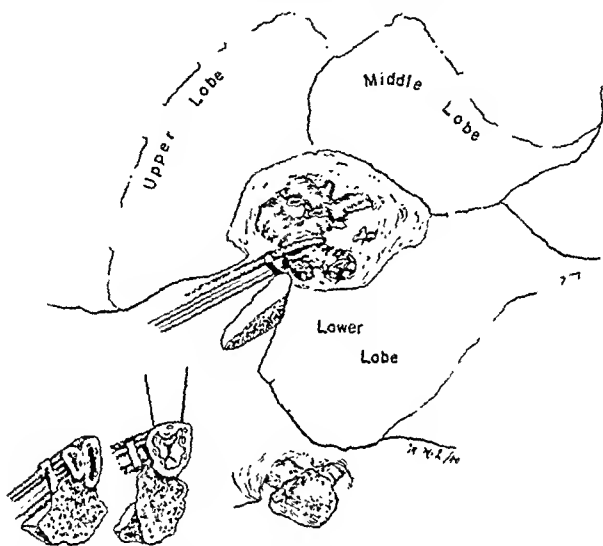


Fig. 7.—After division of arterial supply, the lower lobe bronchus is isolated and grasped with tourniquet. Flap of lung outlined with pedicle for reinforcement of bronchial closure is shown in inserts.

After completion of the fissures the bronchus is isolated and grasped with the tourniquet at the level of the origin of the dorsal segment division (Fig. 7). Care must be taken not to include the bronchus to the middle lobe which may not be seen because of its anterior position. The divided end of the bronchus in the grasp of the cord of the tourniquet will present two orifices, dorsal and basal divisions. These may be converted into one aperture by excision of the carina and then sutured. A flap of lung tissue is used for re-enforcement as described (Fig. 7, inserts).

Right Lower and Middle Lobes: Not infrequently the extent of the disease requires that the middle lobe be resected with the lower lobe. The only further anatomic consideration in such a procedure is that the venous return from the middle lobe is collected by the lowest tributary of the superior pulmonary vein and is found on the anterior aspect of the hilum by retracting the middle lobe and the lower portion of the upper lobe backward (Fig. 8).

Middle Lobe: Resection of the middle lobe alone by individual ligation technique is possible but not recommended. The bifurcation of the middle lobe bronchus occurs at a high level and the blood supply is so complicated that tourniquet technic had best be employed. The hilar stump is so small that the disadvantages of the tourniquet technique would be more theoretical than practical.

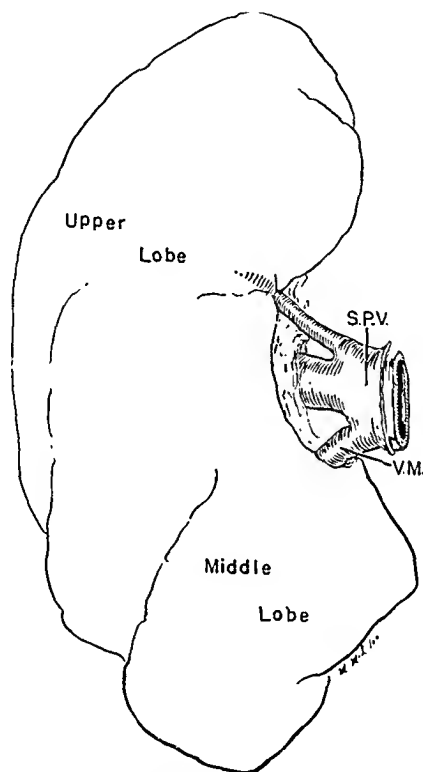


Fig. 8.—Right hilar dissection from anterior aspect. S. P. V., Superior pulmonary vein; V. M., tributary from middle lobe. Note line of pericardial reflection.

Upper Lobes: Time does not permit a detailed presentation of the surgical anatomy of the intrahilar regions of the upper lobes. In general, by dissecting from above downward, the branches of the pulmonary artery supplying the upper lobe are encountered in sequence and may be individually isolated and divided between ligatures. The major tributaries of the superior pulmonary veins are individually isolated and ligated as the pericardial reflection extends well over the main trunks of these vessels. If the middle lobe is to be preserved, the lowest tributary of the right superior pulmonary vein must be preserved.

Mediastinal (Total) Pneumonectomy.—The techniques of total pneumonectomy by isolation and ligation of the pulmonary vessels within the mediastinum have been so admirably described by a number of writers

(Rienhoff, Crafoord, and others) that they will not be considered in detail. In general I have followed the technique described by Rienhoff² for the closure of the main bronchus. A tourniquet with a round-tipped metal button attached to the end of the staff has been found useful to occlude the bronchus while the sutures are being placed. The button serves as an obturator in the flexible membranous portion of the bronchus and folds it into the rigid, cartilaginous portion. Particularly on the left where it is difficult to reapproximate the pleural edges of the mediastinal defect, it has been my custom to reinforce the closure with a free graft of tissue taken from the periphery of the excised lung.

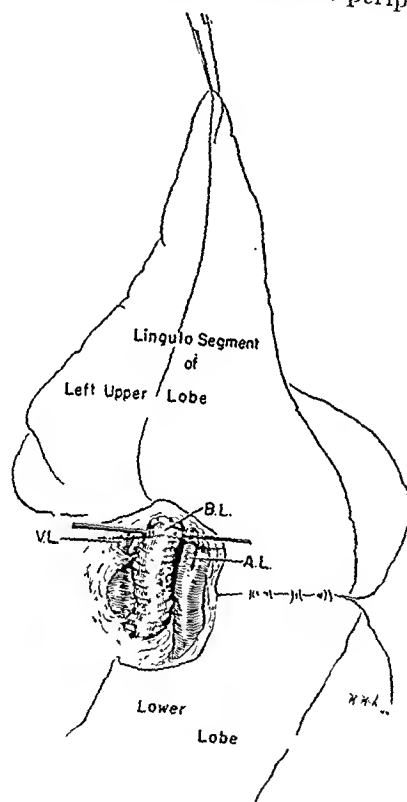


Fig. 9.—Segmental pneumonectomy as applied to lingula segment of left upper lobe. Isolation of bronchus (B. L.), artery (A. L.), and vein (V. L.)

Segmental Pneumonectomy.—The lobe became the surgical unit of the lung because of the technical convenience of the interlobar fissures. Lobectomy is in many instances a concession to operative techniques rather than a resection the extent of which is outlined by underlying pathology. Two years ago I proposed that attention be directed to the bronchovascular segments of the lung as unit structures of surgical importance.⁹ The significance of these segmental divisions in diagnosis and accurate topographic localization has been discussed many times.^{10, 11}

The projections of the major bronchovascular segments on the surface of the lung are easily outlined by injection of the individual branch bronchi. It was pointed out to me by Alfred Goldman that a lung macerated in a weekly corrosive solution tends to separate into these component bronchovascular segments. The artificially produced cleavage planes are not transversed by bronchi but close to the hilum anastomotic blood vessels are found with increasing frequency. The significant fact emerges that a single bronchovascular segment may be dissected from the surrounding lung if its geometric outlines can be visualized, and that the planes of this dissection are not traversed by sizable bronchi and by only a few anastomotic vascular channels.

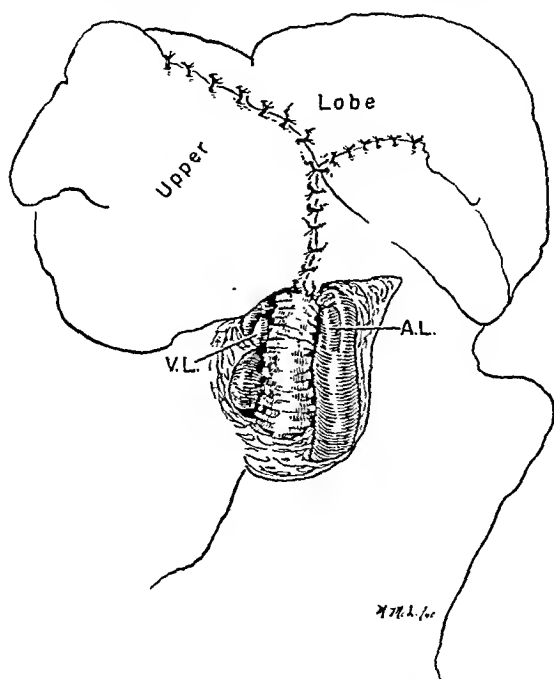


Fig. 10.—Resection of lingula completed. Bronchial stump buried and hemostatic suture line on under surface of upper lobe.

The technical problem involved becomes an exercise in solid geometry, fortunately made easy by resorting to a maneuver that may be referred to as *segmental deflation*. The bronchus and vascular supply of the desired segment are exposed by intrahilar dissection and the vessels ligated (Fig. 9). The anesthetist is then instructed to release the positive intratracheal pressure and the lung is deflated with the aid of gentle manual pressure if necessary. A light clamp or the snare of a tourniquet is then applied to occlude the bronchus. If a tourniquet is used, it is applied only to the isolated bronchus. Positive pressure is then re-established and it will be found that the segment to be resected remains collapsed while the rest of the lung is inflated. The bronchovascular seg-

ment may then be developed by dissection in the plane between collapsed and inflated lung. Curved clamps are used on the divided lung substance to facilitate the placement of hemostatic sutures. When the isolated bronchus is reached it is divided distal to the clamp or tourniquet and secured by suture with plastic reinforcement from adjacent lung tissue (Fig. 10).

Segmental pneumonectomy finds its most common application in the resection of the lingula segment of the left upper lobe in bronchiectasis. It has also been employed to the lower lobe to excise a diseased basal segment and preserve the integrity of a normal dorsal segment. The deflation technique has also been found useful in developing the plane of incomplete interlobar fissures.

Partial Lobectomy and Pneumonectomy.—There remains for consideration the simple removal *en bloc* of a portion of a lobe or lobes, and this problem may be dismissed briefly. When the extent of the lesion or the nature of the underlying pathology does not require or permit one of the formal types of pulmonary resection that I have described, a wedge-shaped segment may be removed from the peripheral portion of the lung and the defect closed by hemostatic sutures. Particularly in suppurative lesions the high frequency cautery or actual cautery may be employed if local or regional anesthesia permits their use. If advisable, the defect may be packed with gauze and allowed to close by granulation with or without the aid of a subsequent plastic procedure. This presupposes fixation of the lung to the parietal chest wall either by pre-existing adhesions, a two-stage operation, or suture.

It will be recalled that bronchial fistulas arising from peripheral portions of the lung and fixed to the chest wall are more apt to remain open than a fistula from the hilar region that lies deeply within the thorax. This is true even though the peripheral fistula is of a much smaller caliber.

APPLICATION OF DESCRIBED TECHNIQUES

Having described the techniques of pulmonary resection, I shall briefly refer to the indications that direct their use in the diseases for which pulmonary resection is commonly employed. In referring to the series of operations on which these conclusions are based, I do not wish to imply that the methods now recommended have been consistently used throughout or, as a matter of fact, will be used for any considerable period in the future. The statistical tables are introduced to give some approximate idea of the comparative risks of pulmonary resection in different diseases and also to illustrate to a limited extent the comparative risks of lobectomy and total pneumonectomy. As stated, a comparative study of tourniquet lobectomy and intrahilar lobectomy is im-

possible at the present time. A more complete discussion of the operative results of segmental pneumonectomy will be found in a previous communication.⁹

Bronchiectasis.—Time does not permit a consideration of the general indications for pulmonary resection in bronchiectasis. This form of treatment is so well established and so generally accepted that discussion is superfluous.¹²

Tourniquet lobectomy has been the most commonly applied technique for bronchiectasis, although recently it has been found that intrahilar lobectomy can be carried out to advantage in a large percentage of cases. Segmental pneumonectomy is applied to the lingula of the upper lobe that requires resection in 80 per cent of patients undergoing left lower lobe lobectomy. If bronchograms show the disease limited to the posteromedial division of the lingula bronchus, resection of the entire lingula is not required. The middle lobe is involved and requires resection with the right lower lobe in many cases. Not infrequently the middle lobe represents the only focus of the disease, or involvement of this lobe may be combined with bronchiectasis of the left lower lobe.

Careful appraisal is advisable before a program of bilateral resection is projected. Even if the bronchi of the lobes that are to remain appear normal, alveolar structure is apt to be damaged by fibrosis and emphysema and its functional capacity reduced to a corresponding degree. In bilateral cases with scattered involvement of several bronchovascular segments, normal lung tissue may be conserved by applying the principle of segmental pneumonectomy to the lower lobes; for example, resecting diseased basal segments and preserving normal dorsal segments. There is probably no good reason at the present time for attempting to divide the lower lobe by this technique unless a bilateral program is under consideration.

Cases of bronchiectasis that require total pneumonectomy are usually so far advanced that individual ligation of the vessels will be found impossible and recourse to tourniquet technique will be necessary.

The immediate results of the application of pulmonary resection in bronchiectasis are summarized in Table I.

Lung Abscess.—The indications for pulmonary resection in lung abscess are still in a formative state and invite discussion. The necrotizing anaerobic infection of putrid lung abscess not infrequently leaves an irreparable defect in the lung. If external drainage is delayed or inadequate and the infection enters the chronic state, there will be found neighborhood foci of bronchiectasis as well as irreversible fibrotic changes. Earlier external drainage will tend to reduce the number of cases showing extensive and irreparable damage, but there will always remain instances of infection that were massive from the time of onset and certain cases that fail to receive adequate care.

TABLE I
PULMONARY RESECTIONS FOR BRONCHIECTASIS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|------------------------|--------|-----------------|------|
| A. Lobectomy* | | | |
| Unilateral | 112 | 2 | |
| Bilateral (6 cases)† | 12 | 1 | |
| | 124 | 3 | 2.4 |
| B. Total pneumonectomy | | | |
| Single stage | 7 | 1 | |
| Lobar stages | 2 | 0 | |
| | 9 | 1 | 11.1 |
| All resections | 133 | 4 | 3.0 |

*Segmental resection of the lingula has not been itemized as a separate procedure when performed with or subsequent to left lower lobectomy. Two cases of segmental resection of the basal segment of left lower lobe and lingula are counted as lobectomies.
†Lt. L. + Rt. M., 3; Rt. L. + Lt. L., 2; Rt. L. + M. + Lt. L., 1.

The problem of lung abscess therapy by no means ends with the establishment of external drainage. In reported studies of end results the number of cases classified as "improved" rather than "cured" is striking. Even though subsequent healing appears sound, recurrences are not rare events. In our experience a recurrent abscess has never been cured by reestablishing drainage.¹³

Pulmonary resection may be undertaken either as a primary procedure or secondary to the establishment of external drainage. As a primary operation it is recommended for consideration in the subacute or chronic phases of the disease when multiple cavities are present or irreparable damage to the lung is apparent. Primary resection should receive consideration in upper lobe abscesses that are notoriously difficult to drain without undue mutilation of the shoulder girdle musculature or that may require subsequent thoracoplasty to bring about healing. Recurrent hemorrhage either before or after external drainage may make resection a procedure of necessity if not of choice.

In general, the reflection of a serious bout of infection on the constitution of the patient will speak for drainage as the first step in surgical treatment. As the active infection subsides, the damage may be more precisely assayed and resection employed as a measure to promote healing. I have not been at all satisfied with the use of muscle flap implantations or other form of plastic closure of residual lung abscess defects. Pedicle muscle grafts are permanently successful in my hands only if the cavity is unilocular, if it possesses flexible walls, and if there is no adjacent bronchiectasis. Under these conditions healing will usually occur spontaneously if the cavity has been adequately unroofed and drainage is maintained for a longer space of time.

In carrying out a primary resection for lung abscess, it is recommended that unusual precautions be taken to avoid emptying the abscess

contents into the bronchial tree. This may be avoided by immediate placement of a tourniquet around the hilum before mobilizing the adherent lung. If a barrier of adhesions prevents this maneuver, the outer shell of the abscess cavity may be incised and its contents evacuated by suction, accepting the added contamination of the pleural cavity that is entailed. The cavity of a large abscess will usually be entered later during the amputation of the lobe so the factor of contamination is relatively unimportant.

The edema of acute infection and the hyperplasia of bronchial lymph nodes makes intrahilar isolation of the pulmonary blood vessels impractical or actually hazardous, so tourniquet technique is recommended also for this reason. Dilatation of vessels reaching the lung from the systemic circulation, not only the bronchial arteries but small arteries from the mediastinum, makes special care in the suture of the stump imperative.

Abscesses that present on the surface of an interlobar fissure or that have crossed a fissure and extended into an adjacent lobe require special comment. A portion of the outer wall of an abscess cavity may be left adherent to an adjacent lobe if development of the fissure means damage to the normal lung. If the abscess extends into another lobe, the involved area may be excised *en bloc* or left widely opened to drain into the empyema cavity. If involvement of the adjacent lobe is extensive, total pneumonectomy may be indicated and carried out immediately or in lobar stages.

When pulmonary resection is undertaken secondary to external drainage of a lung abscess, the operation should be postponed until the manifestations of active infection have subsided. If drainage is perfect, these patients often regain a state of robust health, although they are apt to experience periodic exacerbations of infection or recurring episodes of hemoptysis or hemorrhage from a persisting bronchoenteric fistula.

In a secondary operation mobilization of the lobe is usually readily accomplished once the zone of dense adhesions that surrounds the window in the chest wall is passed. Amputation by tourniquet technique is recommended because the fibrosis of the perivasenar lymphatics within the hilum offers a barrier to dissection of the blood vessels.

The results of pulmonary resection for lung abscess tabulated in Table II show an increased hazard in operative mortality when compared to the bronchiectasis group. This increased risk is largely due to the more virulent nature of the infection harbored by these patients. Brief reference to the fatal cases illustrates this point.

CASE 1.—Primary tourniquet lobectomy for hemolytic streptococcus abscess (pure culture) of the middle lobe. Death due to generalized streptococcus bacteremia before the days of chemotherapy.

TABLE I
PULMONARY RESECTIONS FOR BRONCHIECTASIS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|------------------------|-----------|-----------------|------|
| A. Lobectomy* | | | |
| Unilateral | 112 | 2 | |
| Bilateral (6 cases)† | 12 | 1 | |
| | <hr/> 124 | <hr/> 3 | 2.4 |
| B. Total pneumonectomy | | | |
| Single stage | 7 | 1 | |
| Lobar stages | 2 | 0 | |
| | <hr/> 9 | <hr/> 1 | 11.1 |
| All resections | 133 | 4 | 3.0 |

*Segmental resection of the lingula has not been itemized as a separate procedure when performed with or subsequent to left lower lobectomy. Two cases of segmental resection of the basal segment of left lower lobe and lingula are counted as lobectomies.

†Lt. L. + Rt. M., 3; Rt. L. + Lt. L., 2; Rt. L. + M. + Lt. L., 1.

The problem of lung abscess therapy by no means ends with the establishment of external drainage. In reported studies of end results the number of cases classified as "improved" rather than "cured" is striking. Even though subsequent healing appears sound, recurrences are not rare events. In our experience a recurrent abscess has never been cured by reestablishing drainage.¹³

Pulmonary resection may be undertaken either as a primary procedure or secondary to the establishment of external drainage. As a primary operation it is recommended for consideration in the subacute or chronic phases of the disease when multiple cavities are present or irreparable damage to the lung is apparent. Primary resection should receive consideration in upper lobe abscesses that are notoriously difficult to drain without undue mutilation of the shoulder girdle musculature or that may require subsequent thoracoplasty to bring about healing. Recurrent hemorrhage either before or after external drainage may make resection a procedure of necessity if not of choice.

In general, the reflection of a serious bout of infection on the constitution of the patient will speak for drainage as the first step in surgical treatment. As the active infection subsides, the damage may be more precisely assayed and resection employed as a measure to promote healing. I have not been at all satisfied with the use of muscle flap implantations or other form of plastic closure of residual lung abscess defects. Pedicle muscle grafts are permanently successful in my hands only if the cavity is unilocular, if it possesses flexible walls, and if there is no adjacent bronchiectasis. Under these conditions healing will usually occur spontaneously if the cavity has been adequately unroofed and drainage is maintained for a longer space of time.

In carrying out a primary resection for lung abscess, it is recommended that unusual precautions be taken to avoid emptying the abscess

Tuberculosis.—The efficacy of collapse therapy at a relatively low risk has kept pulmonary resection for tuberculosis at a minimum. Advance has been made more through operations performed under mistaken diagnoses than by deliberately planned resections.



Fig. 11.—Patient described in Case 3.

At the present time bronchial stenosis is the most suggestive indication for resection in this disease and presents the greatest obstacles for treatment by any other measure. Blocked cavities, either air containing or filled with caseous material that has not found an outlet into the bronchial tree, may offer indications for resection. A third possible indication for extirpation may exist in lesions so situated that the likelihood of closure by collapse therapy is slight. The enthusiast should

SURGERY

TABLE II

PULMONARY RESECTIONS FOR LUNG ABSCESS (EXCLUDING CAUTERY RESECTIONS)
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|--------------------------|----------|-----------------|------|
| A. Primary lobectomy | 12 | 2 | |
| Total pneumonectomy | | | |
| Single stage | 2 | 2 | |
| Lobar stages | 0 | 0 | |
| | <hr/> 14 | <hr/> 4 | 28.5 |
| B. Secondary to drainage | | | |
| Segmental pneumonectomy | 1 | 0 | |
| Lobectomy | 10 | 1 | |
| Total pneumonectomy | | | |
| Single stage | 2 | 0 | |
| Lobar stages | 1 | 0 | |
| | <hr/> 14 | <hr/> 1 | 7.1 |
| All resections | 28 | 5 | 18.0 |

CASE 2.—Primary tourniquet lobectomy for putrid post-tonsillectomy lung abscess of right upper and middle lobes. Sixteen months' duration. Death from contralateral septic pneumonia.

CASE 3.—Primary total pneumonectomy as heroic measure in a malnourished infant with diffuse necrotizing putrid infection of left lung (Fig. 11). Death on table coincident with application of tourniquet.

CASE 4.—Primary pneumonectomy in lobar stages for diffuse necrotizing and putrid post-tonsillectomy lung abscess of five months' duration. Survived right upper and middle lobe resection but infection shown to have crossed fissure to involve dorsal segment of lower lobe. Tourniquet resection lower lobe ten months later with death on table from emptying abscess cavity into tracheobronchial tree during mobilization of lobe.

CASE 5.—Tourniquet lobectomy right upper lobe following three drainage operations for multilocular putrid abscess, bronchiectasis, and diffuse pneumonitis of three years' duration. Death from septic bronchopneumonia and empyema.

Cystic Disease.—Both the clinical and pathologic definition of congenital cystic disease of the lung are difficult, and only a few cases have been grouped under this heading. Doubtlessly others have been included under lung abscess or bronchiectasis. The principles that govern pulmonary resections for abscess and bronchiectasis are applicable to cystic disease and need not be repeated. As one death occurred from contralateral pneumothorax occasioned by the perforation of a subpleural cyst of the supposedly sound lung, this consideration should be kept in mind.

Table III probably gives too grave an estimate of the hazards of pulmonary resection in this disorder. The number of cases is too small for appraisal on a percentage basis.

Tumors.—The challenge of neoplastic disease has been second only to the exigencies of wounds of battle in leading surgeons to overstep the limitations of established precedent. Tumors are classified as benign or malignant on the basis of the natural history of their behavior rather than on the basis of whether or not they may prove fatal to the individual patient. It is important to bear this fact in mind in any consideration of pulmonary neoplasms, as a small benign tumor not infrequently produces the fatal sequelae of bronchial obstruction. A classification based on the natural history of the tumor is, however, of great importance in determining the type and magnitude of surgical resection.

During the ten-year period ending April 1, 1940, a clinical diagnosis of primary tumor of the lung was made in 380 cases at the Massachusetts General Hospital.¹⁵ It was confirmed by microscopic examination in 172 cases, of which 155 are classified as primary bronchogenic carcinoma, 15 as adenomas or carcinoids, 1 as neurofibroma, and 1 as hamartoma. The frequency of benign tumors in the entire group is but 4.4 per cent, a relatively insignificant number. The frequency calculated for the group with microscopic confirmation of the diagnosis rises to 10 per cent. If attention is directed to the group in which resection was carried out, it is found that benign lesions account for approximately 30 per cent of resectable bronchogenic tumors. If consideration is still further limited to patients surviving resection with apparent arrest of the disease, benign lesions comprise 64 per cent. These figures are cited to show how important it is for surgeons and pathologists to agree in their definitions before comparing results in the treatment of pulmonary neoplasms.

Bronchial Adenoma (Carcinoid): It is said that this tumor can be adequately handled by bronchoscopic methods, either by extirpation with or without the use of the diathermic electrode, or by the application of radium. In only 4 of 15 cases has this approach been applicable clinically or given satisfactory clinical results. A careful study of the gross lesion in the 11 cases subjected to resection gives convincing evidence of the inadequacy or frank impossibility of eradicating the tumor by endoscopic methods. The extraluminal portion of the tumor is almost invariably of much greater bulk than the intraluminal portion. In addition, the lung distal to the obstructing tumor has suffered irreparable damage.

In our experience lymph node involvement has not been observed as an early or late manifestation of bronchial adenoma. Resection of the tumor itself, therefore, with the segment of lung that has been irreparably damaged appears to be an adequate therapeutic goal. As the tumor rarely is situated distal to the lobar bronchi, lobectomy will be the minimal extent of the resection. In early cases with a minimal degree of infection and lung damage intrahilar lobectomy is advisable as the bronchus must be amputated at a high level. If the tumor impinges

tread on this ground with caution and only after a long experience with modern methods of collapse therapy.

TABLE III
PULMONARY RESECTION FOR CYSTIC DISEASE
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|-------------------------|----------|-----------------|------|
| Lobectomy | 3 | 0 | |
| Segmental pneumonectomy | 1 | 0 | |
| Total pneumonectomy | | | |
| Single stage | 1 | 1 | |
| Lobar stages | 1 | 1 | |
| | <u>6</u> | <u>2</u> | |
| All resections | 6 | 2 | 33.3 |

On theoretic grounds clinical experiments with pulmonary resection in tuberculosis should be limited to cases of chronic isolated bronchogenic phthisis.¹⁴

Resection should be carried out by individual ligation of vessels and suture of the bronchus unless access to the hilar region is absolutely blocked. A limited experience indicates that hilar dissection in tuberculosis is more readily accomplished than in bronchiectasis, due to less inflammatory reaction in the peribronchial lymphatics. Once the primary lesion is established, tuberculous foci in an organ do not produce a lesion in the corresponding lymph nodes.¹⁴ It may also be pointed out that pre-existing pleural effusion attending artificial pneumothorax therapy may result in an almost bloodless cleavage plane as contrasted with areas in which a diseased lung has remained in contact with the parietal chest wall. A preceding pleural effusion, therefore, is in no way a contraindication and may indeed provide strategically favorable conditions.

A limited experience with pulmonary resection in tuberculosis is recorded in Table IV.

TABLE IV
PULMONARY RESECTION FOR TUBERCULOSIS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|---------------------|----------|-----------------|----|
| Lobectomy | 2 | 0 | |
| Total pneumonectomy | 2 | 1 | |
| Single stage | 1* | 0 | |
| Lobar stages | <u>5</u> | <u>1</u> | |
| All resections | 5 | 1 | 25 |

*Preoperative diagnosis of bronchiectasis.

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upon the orifices of other lobar bronchi, as is often the case, total pneumonectomy is required. In long-standing infection with a barricade of hilar fibrosis tourniquet amputation of the lung may be required, even at the cost of leaving the tumor in situ for later resection if symptoms require it.

Other benign tumors are rarities that may be handled by as conservative methods as their size and location permit (Table V).

TABLE V
PULMONARY RESECTION FOR BENIGN TUMORS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|-----------------------|----------|-----------------|------|
| Carcinoid ("adenoma") | | | |
| Lobectomy | 5 | 1 | |
| Total pneumonectomy | | | |
| Single stage | 3 | 0 | |
| Lobar stages | 1 | 1 | |
| | <u>9</u> | <u>2</u> | 22.2 |
| Hamartoma | | | |
| Partial lobectomy | 1 | 0 | |
| Neurofibroma | | | |
| Lobectomy | 1 | 0 | |
| | <u>2</u> | <u>0</u> | |
| All resections | 11 | 2 | 18.1 |

Bronchogenic Carcinoma: Of 156 primary malignant tumors of the lung confirmed microscopically, 155 have been carcinomas and 1 has been sarcoma. The single case of sarcoma was treated by total pneumonectomy and is well. Of the 155 cases of primary carcinoma, operation appeared feasible in 52 (33.6 per cent). Twenty-five cases were proved inoperable by thoracotomy and resection was carried out in 27 (17.4 per cent). Fifteen of the 27 subjected to resection died in the hospital and 7 have died subsequently of their disease. There are now living 5 patients with no apparent residual or recurrent disease (Table VI).

These results are very similar to those reported by Edwards,¹⁶ who notes a salvage of 6 patients out of a total of 172 cases. They are not far different from the situation that is found in carcinoma of the stomach where a salvage of 10 five-year cures out of a total of 200 cases is a representative result.¹⁷

In a consideration of the type of resection that is to be carried out for primary carcinoma of the lung, the problem of the removal of regional lymph nodes comes immediately to attention. The ideal operation for cancer in other organs has been established as the total resection of the organ and the removal *en bloc* of regional lymphatics. An exception, im-

portant by analogy, may be noted in the case of the stomach, as total gastrectomy is commonly performed only when the site of the primary growth demands sacrifice of the cardia.

In proposing total pneumonectomy as the only acceptable procedure for carcinoma of the lung one must take into consideration the differential operative mortality rate of the complete operation as contrasted with that of lobectomy. It will also be recalled that the possibility of a lasting arrest of malignant disease diminishes to a discouraging degree once involvement of the lymph nodes has occurred, so relatively few patients may be saved by even the most radical procedures. The lymphatic system of the hilar region is exceedingly complex and poorly designed for precise surgical dissection.

When total pneumonectomy is proposed in order to remove more adequately a potentially invaded lymphatic area, the question may be framed in simple terms: What price is paid in operative mortality for a few additional centimeters of regional lymphatics? In the greater number of cases of bronchogenic carcinoma this question will not be raised because either the anatomic site of the primary tumor in the hilar bronchi will demand total pneumonectomy, or gross invasion of hilar nodes will call for an attempt to remove them. I refer only to a limited group of cases with peripheral tumors and without gross involvement of regional lymphatics. In these instances I continue to advise lobectomy.

Lobectomy and total pneumonectomy for carcinoma should be carried out by intrahilar and mediastinal dissection technique. Recourse to tourniquet amputation is to be condemned except under unusual circumstances.

TABLE VI
PULMONARY RESECTIONS FOR MALIGNANT TUMORS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|---------------------|----------|-----------------|------|
| A. Primary | | | |
| Sarcoma | | | |
| Total pneumonectomy | 1 | 0 | |
| Carcinoma | | | |
| Lobectomy | 7 | 2 | |
| Total pneumonectomy | 21 | 14 | |
| | <hr/> 29 | <hr/> 16 | 55.0 |
| B. Metastatic | | | |
| Partial lobectomy | | | |
| Unilateral | 1 | 0 | |
| Bilateral (1 case) | 2 | 0 | |
| Lobectomy | 2 | 0 | |
| Total pneumonectomy | 1 | 0 | |
| | <hr/> 6 | <hr/> 0 | 0 |
| All resections | 35 | 16 | 45.7 |

Metastatic Tumors: The status of pulmonary resection for known metastatic tumors of the lung is admittedly one of experimentation. In general, it may be taken under consideration when a solitary metastasis of a tumor of relatively low grade malignancy appears in the lung after complete eradication of the primary growth. It is also to be considered in cases of hypernephroma with a solitary pulmonary metastasis.¹⁸

Resection of metastatic tumors is usually a simple matter technically as the complications of infection that are found in primary tumors are absent. Peripheral nodules may be removed *en bloc* and larger growths resected by lobectomy or pneumonectomy with intrahilar or mediastinal dissection. Metastases to the bronchial wall may closely simulate primary bronchogenic carcinoma as the signs and symptoms of bronchial encroachment result.

TABLE VII
ALL PULMONARY RESECTIONS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|------------------|--------|-----------------|------|
| Bronchiectasis | 133 | 4 | 3.0 |
| Lung abscess | 28 | 5 | 18.0 |
| Cystic disease | 6 | 2 | 33.3 |
| Tuberculosis | 5 | 1 | 25.0 |
| Benign tumors | 11 | 2 | 18.1 |
| Malignant tumors | 35 | 16 | 45.7 |
| | 218 | 30 | 13.8 |

TABLE VIII
ALL PULMONARY RESECTIONS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|----------------|--------|-----------------|------|
| Lobectomy | | | |
| Partial | 6 | 0 | |
| Complete | 166 | 9 | |
| | 172 | 9 | 5.2 |
| Pneumonectomy | | | |
| Single stage | 40 | 19 | |
| Lobar stages | 6 | 2 | |
| | 46 | 21 | 45.6 |
| All resections | 218 | 30 | 13.8 |

CONCLUSION

Tables VII and VIII summarize the experience of the past ten years with various types of pulmonary resection performed for diseases that commonly present indications for surgical therapy.

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TABLE VIII
ALL PULMONARY RESECTIONS
(10-YEAR PERIOD)

| | NUMBER | HOSPITAL DEATHS | % |
|----------------|------------|-----------------|-------------|
| Lobectomy | | | |
| Partial | 6 | 0 | |
| Complete | 166 | 9 | |
| | <u>172</u> | <u>9</u> | 5.2 |
| Pneumonectomy | | | |
| Single stage | 40 | 19 | |
| Lobar stages | 6 | 2 | |
| | <u>46</u> | <u>21</u> | 45.6 |
| All resections | <u>218</u> | <u>30</u> | <u>13.8</u> |

CONCLUSION

Tables VII and VIII summarize the experience of the past ten years with various types of pulmonary resection performed for diseases that commonly present indications for surgical therapy.

palliative procedure in the alleviation of manifestations.¹⁶³ It has also been claimed that life may be prolonged a few months. King⁸⁷ found that the average duration of life in those cases treated by irradiation was 15.4 months as compared with 9.3 months for the entire series. In 59 cases treated by irradiation, Chandler and Potter²⁹ found that the average duration of life was 11 months; whereas, in 61 untreated cases it was 6 months. Similarly, Ormerod¹¹⁸ also observed a slight increase in duration of life of the treated series. The only case reported that has lived 5 years following irradiation therapy is that of Harper.⁶⁷ On the other hand, Brock,²⁶ who is of the opinion that irradiation therapy is of little value in prolonging life, refers to a case in which the patient lived 8 years after onset of symptoms without any treatment. In fact, there is some evidence that irradiation therapy actually may be detrimental.^{25, 104, 127} Overholt¹²⁷ found that the average duration of life in a series of cases treated by irradiation was 5.6 months; whereas, the untreated cases lived 8 months. Saupe¹⁴⁵ observed that 50 per cent of the patients in a series of 200 cases treated by irradiation died in the first 3 months after treatment and only 15 per cent showed any improvement. We agree with numerous other investigators¹⁶⁴ that irradiation therapy in primary carcinoma of the lung is of little, if any, value.

Whereas it is now generally agreed that surgical treatment is the only form of curative therapy, apparently some^{41, 95, 111, 155} are not yet convinced that total removal of the involved lung is the procedure of choice. These believe that lobectomy is indicated in selected cases. As previously emphasized, it is our firm conviction that any procedure short of total removal of the involved lung is irrational and only by total pneumonectomy can the primary focus as well as the regional lymph nodes be adequately removed. Obviously lobectomy does not permit extirpation of the regional lymph nodes and the significance of this fact is clearly emphasized by the high incidence of lymph node involvement. In a series of 2,579 collected cases the regional lymph nodes were involved in 75.9 per cent. That this is not a theoretical argument is shown by the fact that in Forni's⁵⁶ collected cases of pneumonectomy the incidence of recurrence was 9 per cent in contrast to 25.8 per cent following lobectomy.

Operability.—The operability in carcinoma of the lung is dependent upon a number of factors. Everything else being equal, the operability, as in carcinoma elsewhere, depends upon the length of time which has elapsed since the onset of symptoms. Many of the cases which have been allowed to progress for a considerable period of time are inoperable when they are first seen by the physician. Factors which preclude the possibility of resection are distant metastases; involvement of the contralateral lung; evidence of advanced mediastinal involvement, as indicated

SURGICAL CONSIDERATIONS OF PRIMARY CARCINOMA OF THE LUNG

REVIEW OF THE LITERATURE AND REPORT OF 19 CASES

ALTON OCHSNER, M.D., AND MICHAEL DEBAKEY, M.D.,
NEW ORLEANS, LA.

(From the Department of Surgery, School of Medicine, Tulane University)

THE thoroughly deserved increasing attention and relatively recent revival of interest in primary carcinoma of the lung are probably due to several factors. Of these the most important are the apparently increasing incidence, the relative frequency, the rapid advances in thoracic surgery, and the demonstrated feasibility of surgical therapy. The relatively high incidence of carcinoma of the lung has been insufficiently realized. At present, according to a number of statistical studies,^{23, 27, 28, 28} the lung ranks second in frequency only to the stomach as the primary site of cancer. At Charity Hospital in New Orleans among the necroscopies performed during the past year carcinoma of the lung occurred more frequently than carcinoma of the stomach.²⁹ Yet, only three decades ago, Adler,⁴ who reviewed the literature on the subject, stated: "On one point, however, there is nearly complete consensus of opinion and that is that primary neoplasms of the lung are among the rarest forms of the disease." Whether this phenomenal rise in incidence is due to an apparent or a real increased frequency is still controversial. In a previous publication¹⁷ an extensive review of this phase of the subject was presented and on this basis we are of the opinion that the increase is actual and not only apparent. Of even greater practical significance is the factor of therapy. In the short span of approximately a decade the prognosis in this condition has been reversed from absolutely hopeless to relatively favorable. There are records now of a number of patients living and well five years or more after operation. This has been due chiefly to the rapid strides that have been made in the technical development of thoracic surgery. In fact, these developments have evolved now to such a perfected state that the most important consideration lies in the establishment of early diagnosis.

Whereas in the past there has been some controversy among surgeons and radiologists concerning the relative therapeutic values of operative removal and irradiation in malignancies, at present it is the general consensus that the only curative treatment of primary carcinoma of the lung is surgical extirpation. In inoperable and absolutely hopeless cases irradiation therapy may be of value as a

best operative approach is an anterior one. Another decided advantage of preoperative pneumothorax is the gradual compression of the pulmonary capillary bed which gives the right heart a chance to compensate for the increased peripheral resistance in this area, thus mitigating the sudden change which occurs following the cutting off of the blood supply to the involved lung at the time of ligation of the pulmonary vessels. This is particularly true in elderly patients whose cardiac reserve is diminished and in whom malignancy of the lung is likely to occur. Edwards⁴⁸ has emphasized that an additional advantage of the preliminary artificial pneumothorax is that it permits the determination of the ability of the patient to carry out respiratory function with one lung by compressing the normal remaining parts of the affected lung. He also believes that the opening of the pleural cavity at the time of operation is accomplished with less discomfort to the patient if a preliminary artificial pneumothorax has been done. We have not used the intrapleural injection of beef broth as suggested by Rienhoff,¹³⁴ which presumably increases the reaction of the pleura and prevents infection. Recently this procedure has been successfully used by Samson and Holman.¹⁴²

Another preparatory measure consists in the general rehabilitation of the patient. It is important to place the patient on a high vitamin, high caloric diet. Because of the frequency of an associated infection and consequent vitamin C deficiency, it is essential that these patients be given large doses of ascorbic acid. Generally we administer at least 500 mg. daily for a week or ten days prior to the operation. In addition to this they are given thiamin chloride in approximately 30 mg. doses daily for the same period of time. This latter increases the appetite and gets them in better physical condition. As patients with pulmonary carcinoma usually have an anemia because of the associated infection and hemorrhage, transfusion of whole blood should be given preoperatively. At the time of operation it is necessary to have two or three available donors, because prolonged bleeding may follow division of extensive adhesions and because of the possible accidental massive hemorrhage in which administration of blood during operation is frequently lifesaving.

The problem of anesthesia in intrathoracic surgery is a most important consideration. No attempt will be made here to discuss in detail this phase of the subject as this has been adequately reviewed in previous publications.^{13, 14, 51, 71, 76, 98} Suffice it to say that the most important desiderata are complete control of intrapulmonic pressure, adequate facilities for aspiration of secretions in the respiratory passages during the operation, the maintenance of quiet respirations and high oxygenation, the avoidance of distressing cough reflex, and the rapid return to consciousness following completion of the operation. It is

by marked widening of the mediastinal shadow in roentgenograms; fixation of the trachea and bronchi and widening of the carina as well as extension of the neoplastic process above the bifurcation, as determined bronchoscopically; involvement of either the phrenic or vagus nerves, as indicated by paralysis of the diaphragm and vocal cords respectively; and extension of the neoplastic process to the pleura, demonstrated by thorascopic examination and by the presence of malignant cells in the aspirated pleural fluid. In addition to the manifestations of involvement by the malignant process itself, debility and advanced age are contraindications to radical extirpation.

Whereas most of the factors mentioned above are evidences of inoperability, widening of the carina and apparent fixation of the trachea and bronchi in themselves are not justification for omitting exploration, because occasionally one is agreeably surprised to find that the apparent mediastinal involvement is on an inflammatory basis and that extirpation of the involved lung together with the inflammatory mediastinal nodes is possible. On the other hand, apparently operable cases occasionally will be found inoperable at exploration because of involvement of important mediastinal structures by the neoplastic process or because of the impossibility of completely removing the tumor. *It is our firm conviction, however, that borderline cases should always be given the benefit of exploration even at the risk of closing up a relatively large number without removing the tumor, because it is the only means by which operability can be absolutely determined in these instances.* The operability in carcinoma of the lung is still far too low, probably due to the fact that the diagnosis is not made early. In 139 collected cases^{9, 26, 48, 127, 133} 68 (49 per cent) were operable; whereas, in our series of 30 cases 19 (63.3 per cent) were operable. Our higher operability incidence is probably due to the fact that we have explored cases which apparently were inoperable, but in which we found at the time of operation that a satisfactory extirpation of the involved lung and regional lymph nodes could be done.

As previously emphasized, we are convinced that a preliminary artificial pneumothorax is extremely desirable in the preparation of these patients for pneumonectomy. Generally one to two weeks are required to complete the pneumothorax, which is done in stages, increasing the amount of intrapleural pressure gradually until the pressure is definitely on the positive side. Preoperative pneumothorax is of diagnostic importance in determining the presence, extent, and location of adhesions, thus permitting the preoperative planning of the operative procedure. It is desirable also following pneumothorax to take roentgenograms with the patient in the head-down position in order to determine more clearly the extent of adhesions between the base of the lung and diaphragm. In cases in which there are extensive basal adhesions, a posterolateral approach is preferable; and in cases in which there are apical adhesions, the

best operative approach is an anterior one. Another decided advantage of preoperative pneumothorax is the gradual compression of the pulmonary capillary bed which gives the right heart a chance to compensate for the increased peripheral resistance in this area, thus mitigating the sudden change which occurs following the cutting off of the blood supply to the involved lung at the time of ligation of the pulmonary vessels. This is particularly true in elderly patients whose cardiac reserve is diminished and in whom malignancy of the lung is likely to occur. Edwards⁴⁸ has emphasized that an additional advantage of the preliminary artificial pneumothorax is that it permits the determination of the ability of the patient to carry out respiratory function with one lung by compressing the normal remaining parts of the affected lung. He also believes that the opening of the pleural cavity at the time of operation is accomplished with less discomfort to the patient if a preliminary artificial pneumothorax has been done. We have not used the intrapleural injection of beef broth as suggested by Rienhoff,¹³⁴ which presumably increases the reaction of the pleura and prevents infection. Recently this procedure has been successfully used by Samson and Holman.¹⁴²

Another preparatory measure consists in the general rehabilitation of the patient. It is important to place the patient on a high vitamin, high caloric diet. Because of the frequency of an associated infection and consequent vitamin C deficiency, it is essential that these patients be given large doses of cevitamic acid. Generally we administer at least 500 mg. daily for a week or ten days prior to the operation. In addition to this they are given thiamin chloride in approximately 30 mg. doses daily for the same period of time. This latter increases the appetite and gets them in better physical condition. As patients with pulmonary carcinoma usually have an anemia because of the associated infection and hemorrhage, transfusion of whole blood should be given preoperatively. At the time of operation it is necessary to have two or three available donors, because prolonged bleeding may follow division of extensive adhesions and because of the possible accidental massive hemorrhage in which administration of blood during operation is frequently lifesaving.

The problem of anesthesia in intrathoracic surgery is a most important consideration. No attempt will be made here to discuss in detail this phase of the subject as this has been adequately reviewed in previous publications.^{13, 14, 51, 71, 76, 98} Suffice it to say that the most important desiderata are complete control of intrapulmonic pressure, adequate facilities for aspiration of secretions in the respiratory passages during the operation, the maintenance of quiet respirations and high oxygenation, the avoidance of distressing cough reflex, and the rapid return to consciousness following completion of the operation. It is

obvious, therefore, that the availability of a skillful and highly trained anesthetist is essential. Probably in no other operative procedure is this a more important consideration. Moreover, a highly trained anesthetist can greatly facilitate the technical difficulties of the operation by "washing out" the carbon dioxide and thus keeping the patient in relative apnea. Because the operative procedure of pneumonectomy entails the wide opening of the thoracic cage, pulmonary ventilation may be embarrassed. For this reason readily available positive pressure is desirable. This is considerably facilitated by the presence of an intratracheal tube. Moreover, aspiration of secretions in the tracheobronchial tree is more easily performed with an intratracheal tube in place. Whereas in a previous publication we stated that there were certain undesirable features associated with the use of an intratracheal tube, we are now of the opinion that these disadvantages may be obviated by greater care and skill in its introduction. Of particular importance also is the preoperative bronchoscope aspiration of any secretions in the tracheobronchial tree. This will minimize considerably the spillage of retained secretions in the involved lung during the course of the operation. Bronchoscope aspiration should also be done immediately following the completion of the operation. This procedure will decrease considerably the incidence of postoperative pulmonary complications.

Whereas the choice of anesthetic agent appears to be a matter of personal preference, there is unanimity of opinion regarding the fact that it should be one which permits the administration of a high concentration of oxygen. This is possible with both cyclopropane and ether. On the basis of our experience the former is preferable. On the other hand, Beecher¹⁴ is convinced that ether is better.

Whereas the majority of thoracic surgeons have employed general anesthesia for intrathoracic procedures, more recently others^{27, 23, 29, 148} have indicated their preference for local and spinal analgesia. Although we have had no experience with these forms in intrathoracic surgery, we are in complete accord with Beecher^{13, 14} and Blades²⁹ that their dangers and disadvantages do not justify their routine employment.

There are several types of incisions which may be employed and their choice depends to a great extent upon the presence or absence of adhesions. In cases in which there are no adhesions, the anterior approaches, as suggested by Rienhoff^{144, 151} and Overholt,¹²² are preferable because they permit excellent exposure and are less extensive. The Overholt incision is particularly indicated in cases in which there are extensive adhesions between the upper lobe and the parietal pleura. On the other hand, in cases in which there are extensive adhesions between the lower lobe and the posterior parietal pleura or diaphragm,

a better exposure will be obtained by means of a posterolateral approach, because in this way the adhesions can be divided under direct vision by sharp dissection, which is much less traumatizing and will result in less oozing. Moreover, as suggested by Edwards,⁴³ a posterior incision is more expedient in cases with involvement of the lower lobe and an anterior incision is of greater value in cases with involvement of the upper lobe. The anterior approach, as popularized by Rienhoff, consists of a transverse incision over the third intercostal space extending from the lateral border of the sternum to the anterior axillary line. The pectoral muscles are divided and the pleural cavity entered through the third intercostal space. Greater exposure is gained by separating the third and fourth ribs after disarticulating their costochondral junctions. We previously modified this incision by resecting the third rib instead of making an incision in the intercostal space, but have abandoned this because of the difficulty in closing the thoracic wall. Because of the occasional difficulty in getting adequate exposure through the simple incision in the third intercostal space, we consider it desirable to divide the third and fourth costal cartilages in the parasternal portion; if the lesion is high in the upper lobe with extensive adhesions between the visceral and parietal pleurae, division of the second costal cartilage gives adequate exposure (Figs. 1 and 2). It is imperative that the internal mammary vessels should be ligated above and below because considerable hemorrhage can occur from these vessels if they are injured (Fig. 2). Through this incision with division of the costal cartilages, adequate exposure to the hilum of the lung can be obtained and closure of the thoracic cage is greatly facilitated. Another anterior approach which has been quite popular is that suggested by Overholt¹²² and Edwards.⁴⁷ According to the former a curved incision is made extending from about the fifth sternochondral junction below to the anterior axillary line near the clavicle and the breast mobilized upward and medially as a flap. The pectoral muscles are divided in the second interspace through which the pleura is entered and the cartilages of the first to the fifth ribs divided parasternally. The approach employed by Edwards consists of a right-angled incision, beginning parasternally in the region of the second intercostal space, extending caudally to the fifth intercostal space and then laterally in the fifth intercostal space to the axilla. The third, fourth, and fifth costal cartilages are divided and the intercostal structures in the fifth intercostal space are incised. There are two posterior approaches which can be used. The posterolateral begins in the fifth intercostal space in its paravertebral portion and extends anteriorly to the anterior axillary line. This incision is made through the fifth intercostal structures into the pleural cavity (Fig. 3). The paravertebral portions of the fifth and sixth ribs are divided, permitting

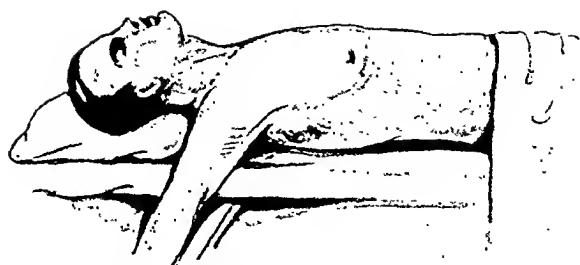


Fig. 1.—Drawing showing position of patient in anterior approach for pneumonectomy. The patient lies in the dorsal position with the arm of the affected side abducted.

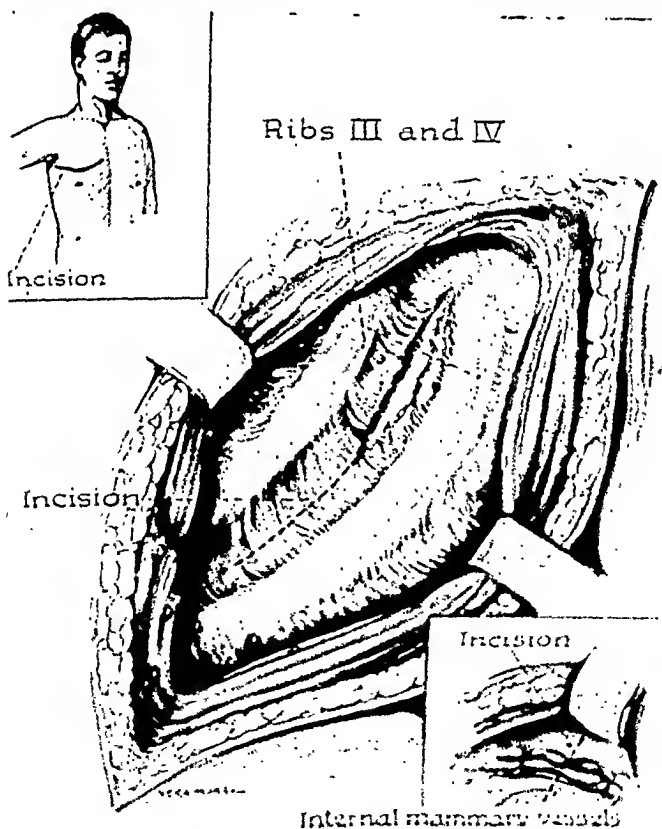


Fig. 2.—Drawing illustrating anterior approach for pneumonectomy. The incision is made transversely over the third intercostal space extending from the lateral border of the sternum to the anterior axillary line. The pectoral muscles are divided and the pleural cavity entered through the third intercostal space. A plexus of veins is frequently observed in the lateral aspect of the incision immediately beneath the pectoral muscles and over the ribs and intercostal muscles. Anticipating hemorrhage from the veins will occur unless preliminary ligation is done. Lower inset shows method of section of the mammary vessels between transverse ligatures.

wider separation. This incision is particularly indicated in cases with lower lobe involvement and with extensive adhesions in this area. A popular incision is that suggested by Crafoord.³⁵ It has the distinct advantage that a wide exposure of the hemithorax is given, but it has the disadvantage that it is an extensive incision and produces considerable trauma. It begins posteriorly in the paravertebral portion of the fourth rib, about 7 to 8 cm. from the posterior midline, extends downward beneath the angle of the scapula, and then up toward the mid-axillary line to the level of the fifth rib which is followed anteriorly to the costal cartilage. After mobilization of the scapula, the fifth rib is resected throughout the entire length of the incision and the pleural cavity entered through its bed.

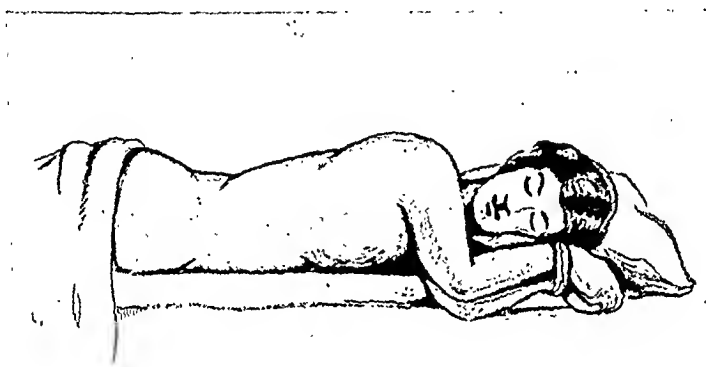


Fig. 3.—Drawing illustrating position of patient in posterolateral approach for pneumonectomy. The incision is made over the fifth intercostal space extending from the paravertebral line to the anterior axillary line.

Following the opening of the pleural cavity and the division of the adhesions by sharp dissection, the hilar structures are exposed in the mediastinum. The hilum is exposed in the mediastinum by incising the mediastinal pleura anteriorly and superiorly in the anterior approach and posteriorly and superiorly in the posterior approach. In the anterior approach care is taken not to injure the phrenic nerve or the accompanying pericardophrenic vessels. The incision is generally made posterior to these structures. Crushing of the phrenic nerve by means of an artery forceps is desirable as it facilitates the operative procedure by producing a hemidiaphragmatic paralysis and is also of value in the early postoperative period by helping obliterate the hemithorax. A flap of mediastinal pleura which is mobilized by the respective incisions is reflected, exposing the hilar structures. The mobilization is greatly facilitated by the use of long, ball-tipped, slightly curved scissors (Fig. 4).

Following mobilization of the mediastinal pleural flaps over the hilum of the lung, the hilar structures are isolated individually. In previous publications great emphasis was placed on this procedure.

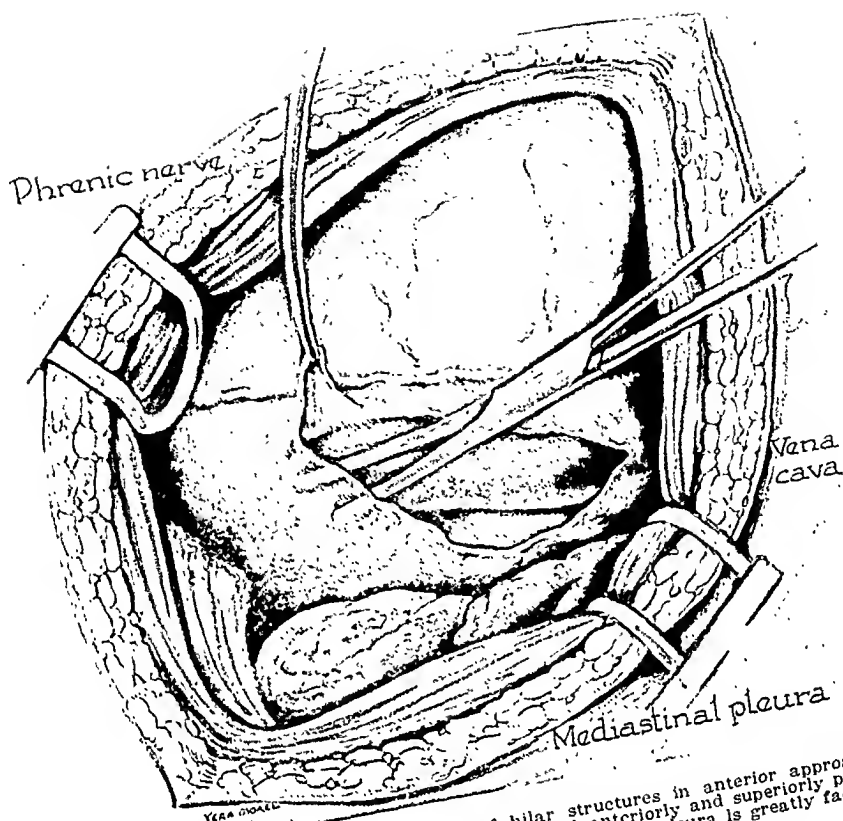


Fig. 4.—Drawing showing exposure of hilar structures in anterior approach for pneumonectomy. The mediastinal pleura is incised anteriorly and superiorly posterior to the phrenic nerve. Mobilization of flaps of mediastinal pleura is greatly facilitated by the use of long, ball-tipped, slightly curved scissors.

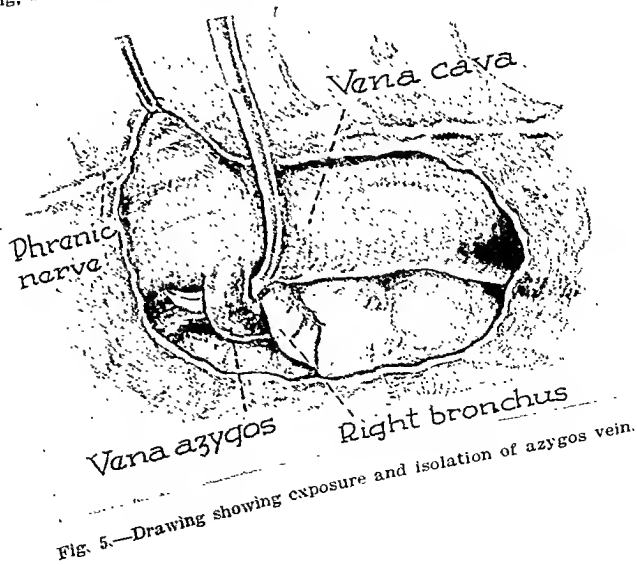


Fig. 5.—Drawing showing exposure and isolation of azygos vein.

Mass ligation of the hilum was condemned as an unsurgical procedure and one which will be followed by bad results in the majority of cases because it does not permit removal of the mediastinal lymph nodes. Moreover, in some cases it does not permit the complete removal of the tumor. In the anterior approach the first structure to be isolated is the pulmonary artery, which is separated from the bronchus and the superior pulmonary vein. However, on the right side, both in the

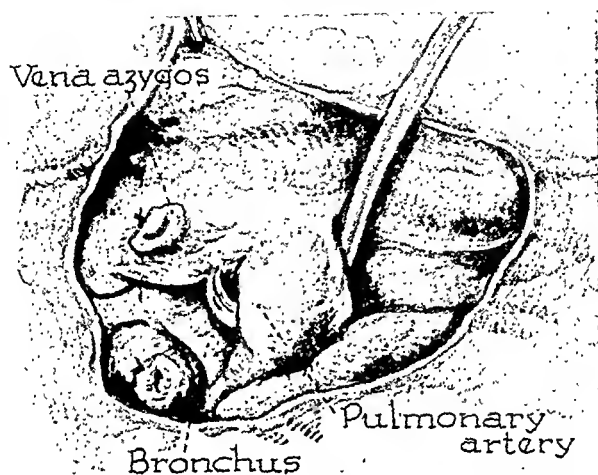


Fig. 6.—Drawing showing exposure and isolation of pulmonary artery. The Semb dissector greatly facilitates carrying ligatures around the hilar vessels.

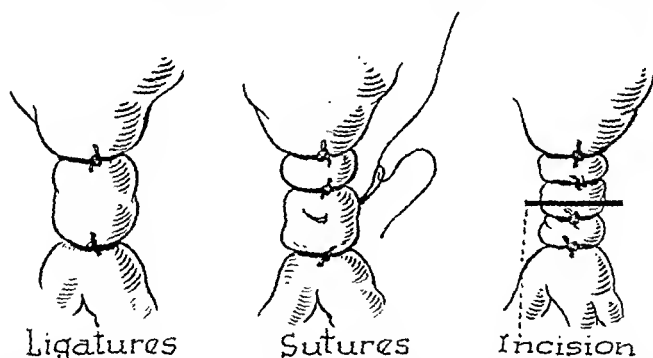


Fig. 7.—Diagrammatic illustration of technique employed in individual isolation and ligation of hilar structures. The pulmonary artery and pulmonary veins are divided between double ligation and transfixion sutures.

anterior and in the posterior approach, as a preliminary procedure, the isolation, ligation, and division of the azygos vein which extends over the right main stem bronchus and in the angle between it and the eparterial bronchus are considered highly desirable (Fig. 5). Failure to do this may lead to its injury with distressing and even fatal hemorrhage. Isolation of the hilar structures is performed principally by blunt dissection using small gauze pledgets and the curved Semb

dissector. After isolation of the pulmonary artery it is doubly transfixed and doubly ligated, following which it is divided between the two transfixed sutures and ligatures (Figs. 6 and 7). Davidson³⁸ recently has described a special ligature-carrier instrument for facilitating the isolation and ligation of the hilar vessels. However, in our experience the Semb dissector has been found most satisfactory (Fig. 6).

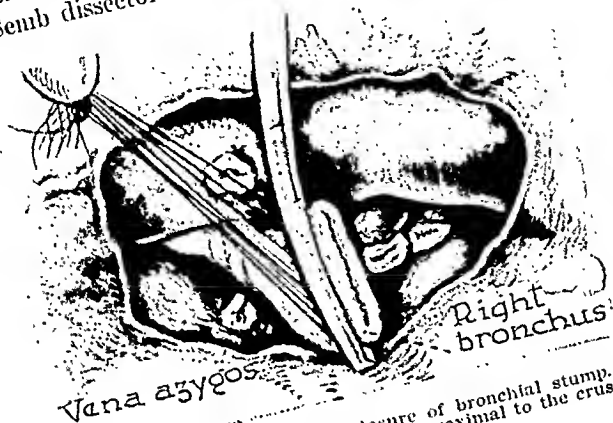


FIG. 8.—Drawing illustrating technique of closure of bronchial stump. The first row of mattress sutures of No. 2 silk is placed just proximal to the crushing clamp.

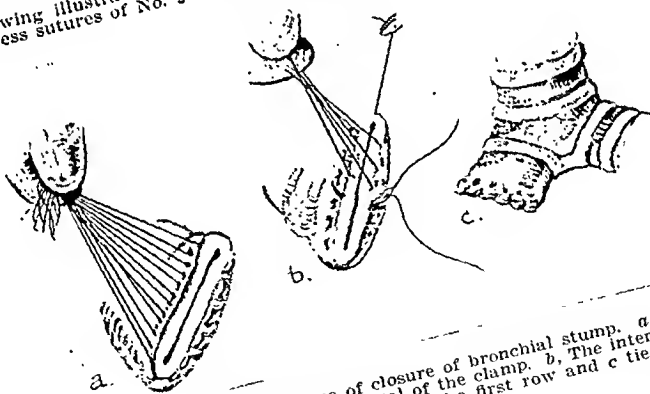


FIG. 9.—Drawing showing technique of closure of bronchial stump. a, The mattress sutures of the first row are tied after removal of the clamp. b, The interrupted sutures of the second row are introduced just distal to the first row and c tied over the end of the bronchus.

It has been clinically and experimentally observed by some that certain cardiac or respiratory disturbances may occur following manipulation and traction on the hilar structures.^{43, 101, 110, 113, 119} Whereas many believe that it is desirable to inject novocain around the hilar structures before their isolation and manipulation, it is our opinion that the occasional manifestations during such a manipulative procedure are due to mechanical factors rather than to reflex stimulation of the vagus or sympathetic nerves. This opinion is based on the fact that in our series of cases, although in the isolation of the hilar structures traction

on the vessels has been done, no disturbances have been observed except in one instance. We agree with Edwards⁵⁰ that traction, particularly on the pulmonary artery, may mechanically compress the main branch and produce these disturbances in cardiac and respiratory action.



Fig. 10.—Photograph of median section of trachea and bronchi of patient dying 12 days after left pneumonectomy of pneumonia and pericarditis. The bronchial stump, which was closed at operation according to the technique described in the text, shows very satisfactory healing.

After division of the pulmonary artery, as suggested by Rienhoff,¹³⁴ it is desirable to isolate the bronchus and pass a ligature around it. This is tightened in order to prevent spillage of the contents within the involved lung into the trachea and the opposite bronchial tree. The superior pulmonary vein is then isolated, doubly transfixed, ligated, and divided. The bronchus is then further freed from its sur-

rounding structures, care being taken not to injure the bronchial vessels. A crushing clamp is placed high on the bronchus just distal to the bifurcation of the trachea. Another clamp is placed just distal to this and the bronchus is divided between the two. The bronchus is closed by means of interrupted silk sutures introduced in two layers.



Fig. 11.—Photograph of median section of trachea and bronchi of patient dying of recurrence 10 months after left pneumonectomy. The excellent closure of the bronchial stump, which was completely lined with mucosa, may be readily observed in spite of the surrounding recurrent carcinomatous tissue.

The first layer is a mattress suture of No. 2 silk, placed just proximal to the clamp (Fig. 8). All of the sutures are introduced before the clamp is removed. After all of the sutures have been installed, extending from one side of the bronchus to the other, the clamp is removed and the sutures are tied. Following this, the interrupted No. 1

silk sutures of a second row are introduced just distal to the first row and tied over the end of the bronchus (Fig. 9). Whereas numerous methods¹⁶⁵ for closure of the bronchial stump have been suggested, many of which are ingenious and complicated, in our experience this has been the most satisfactory (Figs. 10 and 11). The short inferior pulmonary vein is then isolated, doubly transfixed, and ligated. Occasionally, because of the short length of the inferior pulmonary vein, a distal ligation is not practical. In such an instance a crushing clamp is placed in the pulmonary parenchyma just distal to the transfixion

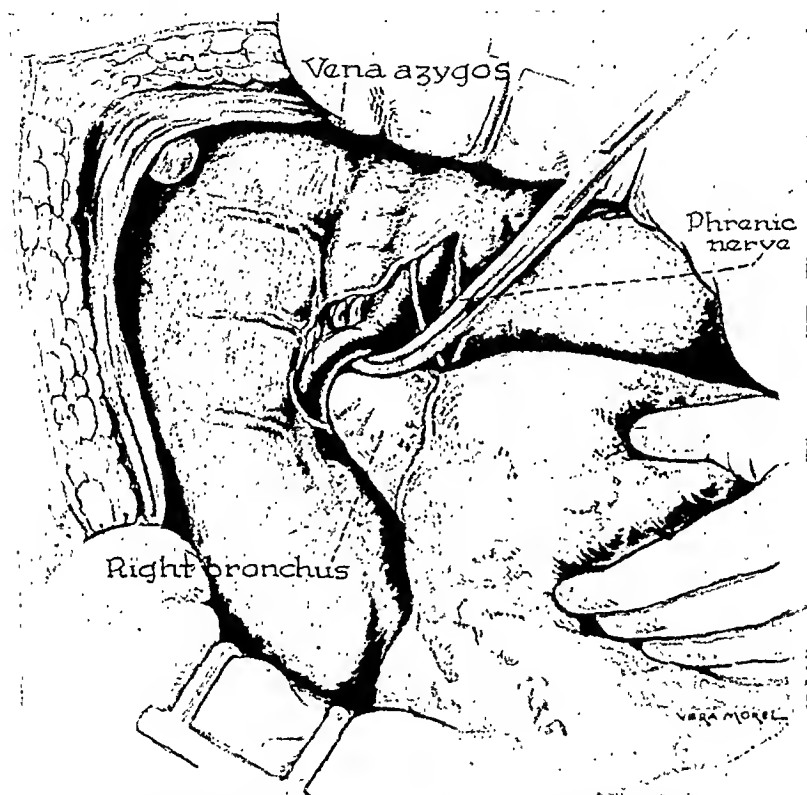


Fig. 12.—Drawing illustrating exposure of hilar structures through posterolateral approach. The mediastinal pleura over the hilum is incised posteriorly and superiorly and the flaps mobilized. The azygos vein is the first structure to be isolated, ligated, and divided.

sutures and ligatures and the vein divided between them. Finally the posterior mediastinal pleura is incised, following which the lung is removed. In the posterior approach the technique of isolation, division, and closure of the hilar structures is similar but the order of approach is different. Here, as anteriorly, the first structure to be divided on the right side is the vena azygos (Fig. 12). Following this the bronchus is isolated, clamped, and divided. The proximal portion of the bronchus is closed, the distal clamp being allowed to remain in place to act as a

rounding structures, care being taken not to injure the bronchial vessels. A crushing clamp is placed high on the bronchus just distal to the bifurcation of the trachea. Another clamp is placed just distal to this and the bronchus is divided between the two. The bronchus is closed by means of interrupted silk sutures introduced in two layers.



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cotton. The retention sutures which are buried are then tied and the pectoral muscles are approximated by means of quilting cotton. The skin edges are brought together with a continuous cotton suture. No drainage is instituted, because we believe with Rienhoff that filling of the pleural cavity with fibrinous exudate is important in the obliteration of the cavity (Figs. 17-19). Thoracoplasty has not been found necessary and subsequently there is little or no disfigurement of the chest (Fig. 20). We have not observed infection except in one case in which the bronchial stump "blew out" in a patient who had received

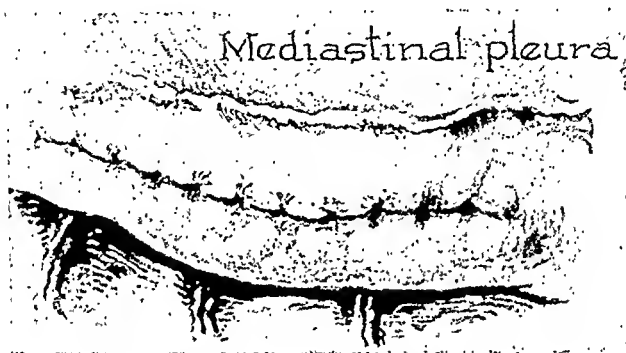


Fig. 15.—Drawing showing pleuralization of mediastinum following complete extirpation of mediastinal lymph nodes. The edges of the mediastinal pleural flaps are approximated, thus covering with pleura the stumps of the ligated vessels and bronchus.

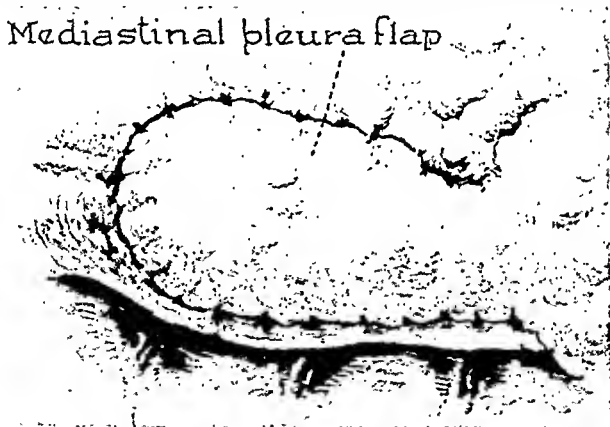


Fig. 16.—Drawing showing methods of covering the stumps of the ligated vessels and bronchus with a mediastinal pleural flap obtained from an adjacent portion of the mediastinum or the pericardium.

a great deal of preoperative irradiation and in whom there was no attempt at healing, both in the mediastinal and in the parietal wounds, presumably due to the extensive irradiation.

After the patient is returned to bed, the foot of the bed is elevated from 12 to 18 inches to facilitate the emptying of the tracheobronchial tree of any secretion. Oxygen is administered by means of a mask, and the patient is given fluids by means of an intravenous drip. Al-

retractor in facilitating exposure of the hilar structures. The pulmonary artery is then isolated, ligated, and divided, following which the superior pulmonary vein and finally the inferior pulmonary vein are similarly treated (Figs. 13 and 14).

After removal of the lung, the mediastinal lymph nodes are extirpated in their entirety. In this way metastases to these structures can be removed. Their deeply pigmented character greatly facilitates their recognition and isolation. If the bronchial vessels have not been ligated previously, this should be done. Following the complete extirpation of all the mediastinal lymph nodes, careful pleuralization of the mediastinum is imperative. The edges of the divided mediastinal pleura are approximated, thus covering with pleura the stumps of the ligated

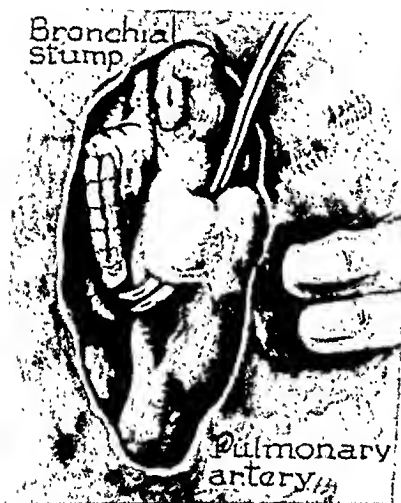


Fig. 13.

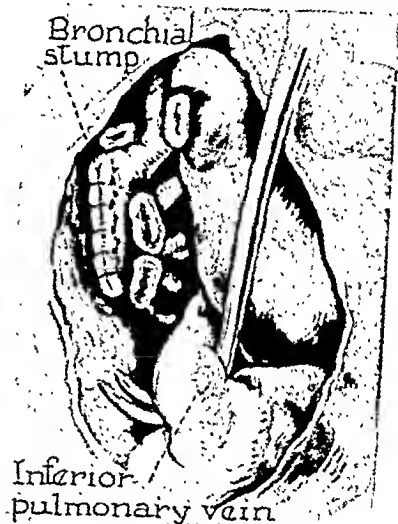


Fig. 14.

Fig. 13.—Drawing illustrating technique of isolation and ligation of hilar structures through posterolateral approach. After ligation and division of the azygos vein the bronchus is exposed and divided between clamps and the proximal stump ligated as previously described. The pulmonary artery is then isolated and divided between ligatures as described in the anterior approach.

Fig. 14.—Drawing illustrating technique of exposure and isolation of the inferior pulmonary vein through posterolateral approach. This is the final structure to be divided, the superior pulmonary vein having been sectioned between ligatures previously.

vessels and bronchus (Fig. 15). The significance of this important step lies in the fact that the danger of infection is minimized and prompt healing of the bronchial stump augmented. In those cases in which a large amount of the mediastinal pleura has been extirpated it is necessary to obtain a flap from an adjacent portion of the mediastinum or the pericardium in order to cover the ligated stumps, as originally suggested by Rienhoff (Fig. 16).

The thoracic wall is closed in layers by first placing No. 3 silk sutures around the adjacent rib or through holes made in the ribs. Following this, the pleura and intercostal muscles are approximated by quilting

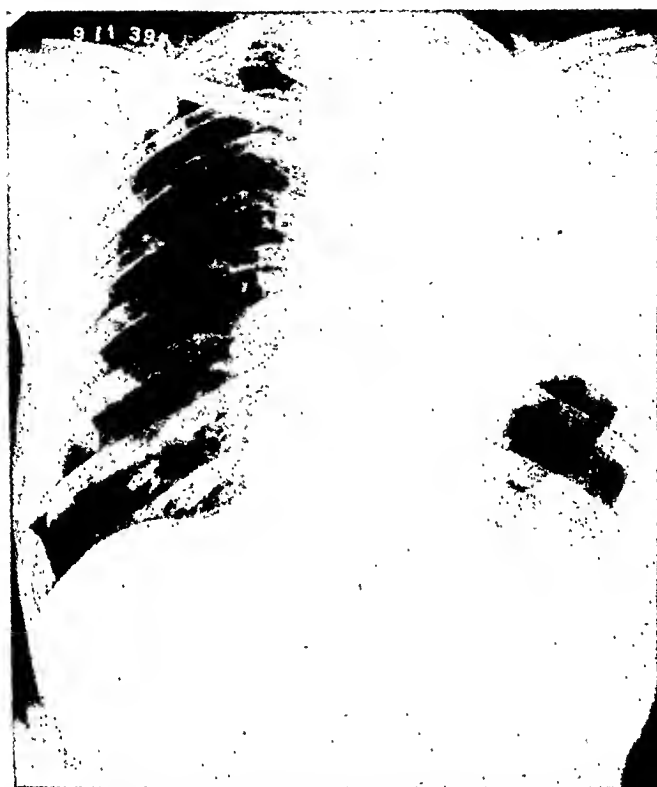


Fig. 19.—Anteroposterior roentgenogram of chest of patient referred to in Fig. 18 taken approximately six weeks after left pneumonectomy. The obliteration of the left pleural cavity is considerably facilitated by the elevation of the left leaf of the diaphragm.

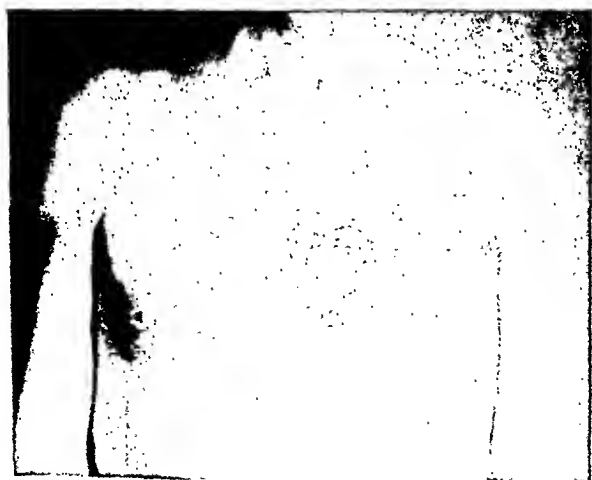


Fig. 20.—Photograph of patient referred to in Figs. 18 and 19 taken approximately 6 weeks after left pneumonectomy. The thin line scar may be observed over the third interspace, but there is no disfigurement of the chest or limitation of motion. The patient is still living and active in his work.



Fig. 17.—Anteroposterior roentgenogram of chest of patient who had left total pneumonectomy 2 years previously for primary sarcoma of left lung. This patient is well now 4½ years after operation with no evidence of recurrence. Roentgenogram shows obliteration of left pleural cavity and shifting of mediastinum to left.

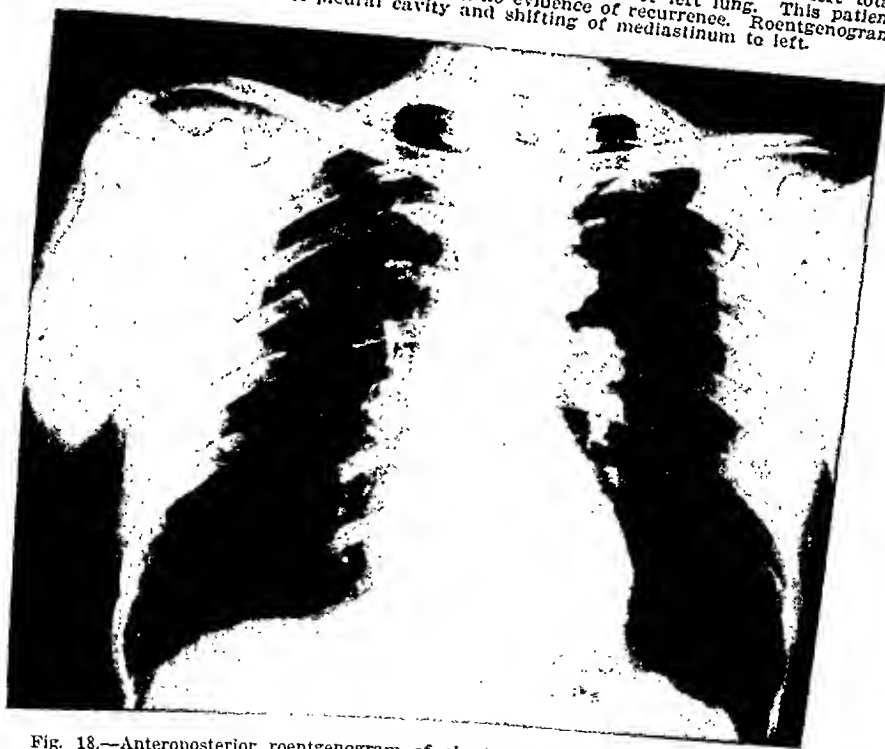
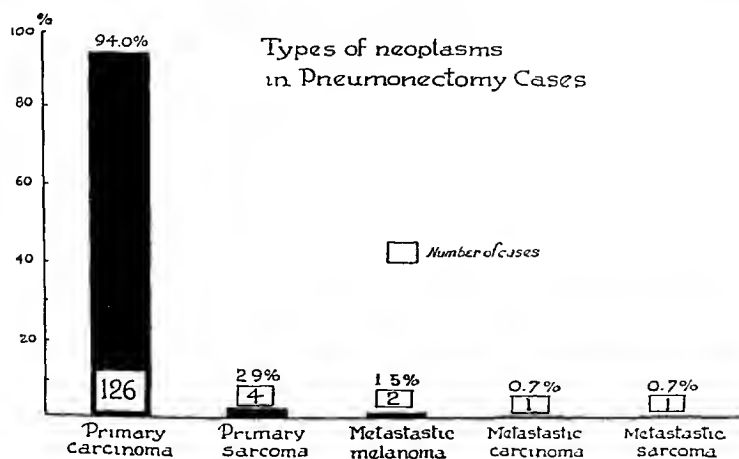


Fig. 18.—Anteroposterior roentgenogram of chest of patient with carcinoma involving left upper lobe bronchus as characterized by rounded irregular shadow near hilum on left side.

significance of this condition. An analysis of these cases reveals some interesting findings.

Of 92 cases in which the sex was stated, 23 (25 per cent) were females and 69 (75 per cent) were males (Graph I). In our series of 19 cases, 4 were in females and 15 were in males. This is somewhat similar to the respective incidences of the previously collected cases¹¹⁵ and approximately the general sex incidence in carcinoma of the lung. In a collected series of 8,575 cases of primary carcinoma of the lung there were 6,769 (79.9 per cent) males and 1,806 (21 per cent) females.^{116, 117} The age of patients was stated in 129 cases. The highest age incidences, 34.8 per cent and 35.6 per cent, were in the fifth and six decades, respectively (Graph II). Of particular interest is the fact that 18.5 per cent, or almost one-fifth, of the cases were below 40 years of age. There were two patients, both with sarcoma, in the first decade, one being 3½ years of



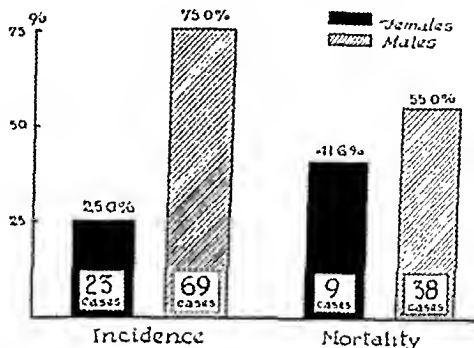
Graph III.—Graphic representation of types of neoplasm in 134 collected cases of pneumonectomy including our cases.

age and the other 5½ years. The oldest patient was 69 years of age. The age incidence in the pneumonectomy cases differs somewhat from the general incidence. For example, in a series of 4,307 collected cases the respective incidences in the fifth, sixth, and seventh decades were 25.4 per cent, 34.1 per cent, and 20 per cent; whereas, in the pneumonectomy cases they were 34.8 per cent, 35.6 per cent, and 10.8 per cent. Thus, in the latter there was a higher incidence in the youngest of these decades and a lower in the oldest. The explanation for this probably lies in the fact that the younger cases are better surgical risks.

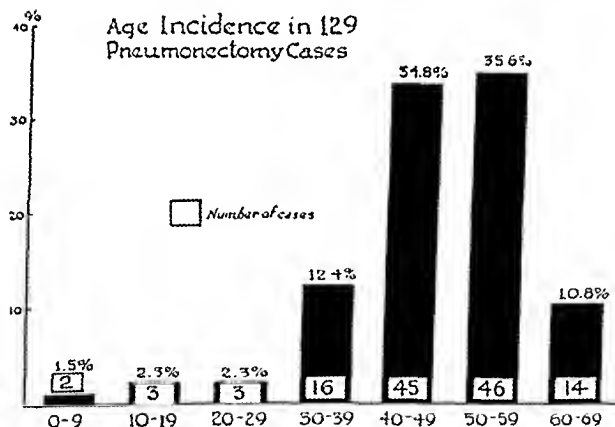
The type of neoplasm was stated in 134 cases and of this number 126 (94 per cent) were primary carcinoma, 4 (2.9 per cent) were sarcoma, 2 (1.5 per cent) were metastatic melanoma, 1 (0.7 per cent) was a metastatic carcinoma, and 1 (0.7 per cent) was a metastatic sarcoma (Graph III).

most invariably after pneumonectomy the patient receives 500 to 1,000 c.c. of whole blood, depending upon the amount of blood lost during the operation. The patient is given adrenal cortical extract every two hours and vitamins C and B are continued during the postoperative period. Only a sufficient amount of morphine to control pain is administered as the depressing effect on the cough reflex is undesirable.

Incidence and Mortality in Pneumonectomy Cases According To Sex



Graph I.—Graphic representation of relative incidence and mortality according to sex in 92 collected cases of pneumonectomy including our cases.



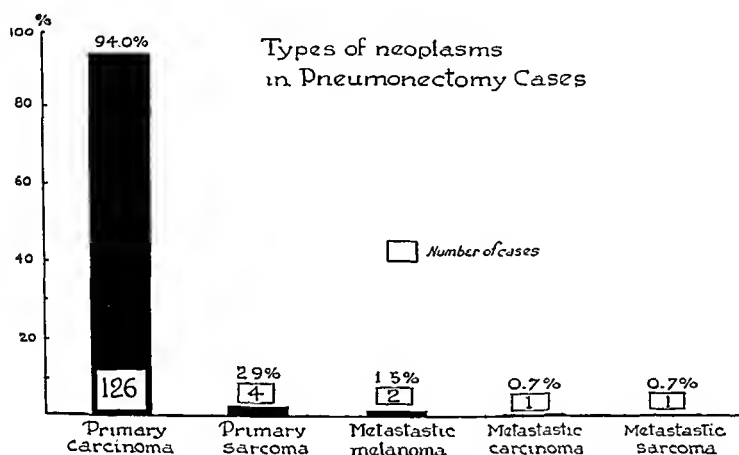
Graph II.—Graphic representation of age incidence according to decades in 129 collected cases of pneumonectomy including our cases.

ANALYSES OF CASES

In a previous publication we¹¹⁵ collected and analyzed 79 reported cases of total pneumonectomy for neoplastic disease. In addition to this number we reported 7 of our own, making a total of 86 cases. Since then there have been reported 60 additional cases and we have had 12 more cases, making a total of 139 collected cases (166) and 19 of our cases, or a grand total of 158 cases. This approximately twofold increase of reported cases of pneumonectomy for malignant disease in a period of less than two years is a gratifying indication of the surgical

significance of this condition. An analysis of these cases reveals some interesting findings.

Of 92 cases in which the sex was stated, 23 (25 per cent) were females and 69 (75 per cent) were males (Graph I). In our series of 19 cases, 4 were in females and 15 were in males. This is somewhat similar to the respective incidences of the previously collected cases¹¹⁵ and approximately the general sex incidence in carcinoma of the lung. In a collected series of 8,575 cases of primary carcinoma of the lung there were 6,769 (79.9 per cent) males and 1,806 (21 per cent) females.^{116, 117} The age of patients was stated in 129 cases. The highest age incidences, 34.8 per cent and 35.6 per cent, were in the fifth and six decades, respectively (Graph II). Of particular interest is the fact that 18.5 per cent, or almost one-fifth, of the cases were below 40 years of age. There were two patients, both with sarcoma, in the first decade, one being 3½ years of

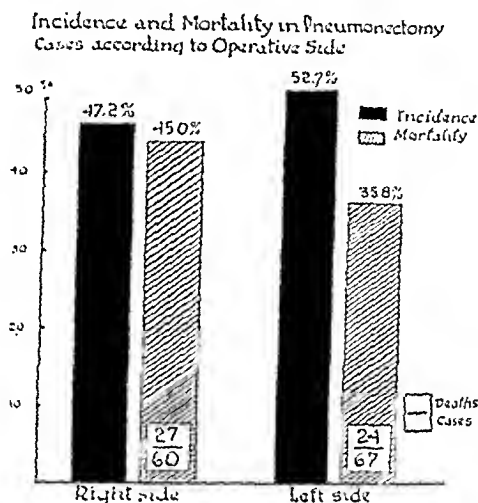


Graph III.—Graphic representation of types of neoplasm in 134 collected cases of pneumonectomy including our cases.

age and the other 5½ years. The oldest patient was 69 years of age. The age incidence in the pneumonectomy cases differs somewhat from the general incidence. For example, in a series of 4,307 collected cases the respective incidences in the fifth, sixth, and seventh decades were 25.4 per cent, 34.1 per cent, and 20 per cent; whereas, in the pneumonectomy cases they were 34.8 per cent, 35.6 per cent, and 10.8 per cent. Thus, in the latter there was a higher incidence in the youngest of these decades and a lower in the oldest. The explanation for this probably lies in the fact that the younger cases are better surgical risks.

The type of neoplasm was stated in 134 cases and of this number 126 (94 per cent) were primary carcinoma, 4 (2.9 per cent) were sarcoma, 2 (1.5 per cent) were metastatic melanoma, 1 (0.7 per cent) was a metastatic carcinoma, and 1 (0.7 per cent) was a metastatic sarcoma (Graph III).

The site of involvement was stated in 127 cases. Of this number 60 (47.2 per cent) were in the right side and 67 (52.7 per cent) were in the left (Graph IV). This is somewhat similar to the previously collected group, but it is in direct contrast to the general incidence in which it has been found that the greatest frequency of involvement is in the right



Graph IV.—Graphic representation of relative incidence and mortality according to operative side in 127 collected cases of pneumonectomy including our cases.

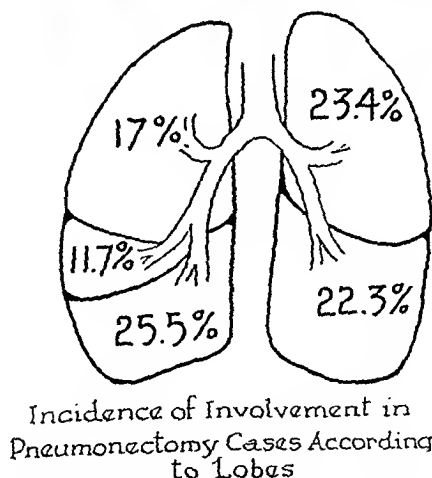
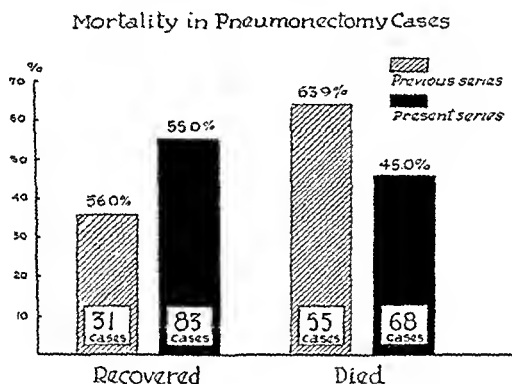


Fig. 21.—Diagrammatic representation of incidence of involvement in pneumonectomy cases according to lobes.

lung. Thus, in a collected series¹¹⁷ of 4,732 cases, 2,761 (58.3 per cent) involved the right lung and 1,971 (41.6 per cent) involved the left. Whether left lung lesions are more likely to be operable is of speculative interest. The involvement according to lobes was stated in 79 cases. The greatest incidence, 25.5 per cent, was found to be in the right lower

lobe and the next in order of frequency, the left upper, the left lower, the right upper, and the right middle (Fig. 21). This also differs from the general incidence of involvement. In an analysis of 784 cases Fischer⁵⁴ found that the right upper lobe was most frequently involved and the next in order of frequency were the left upper, right lower, left lower, and middle lobes.

Of the total number of 151 cases in which the results of the operation were stated, 83 (55 per cent) recovered and 68 (45 per cent) died (Graph V). In the previously collected series the mortality was 63.9 per cent. Thus, the general mortality in a period of less than two years has been reduced almost one-fifth. This gratifying fact clearly reflects the rapid advances in thoracic surgery and favorably indicates that with greater experience in this difficult surgical endeavor the mortality undoubtedly will be further decreased.

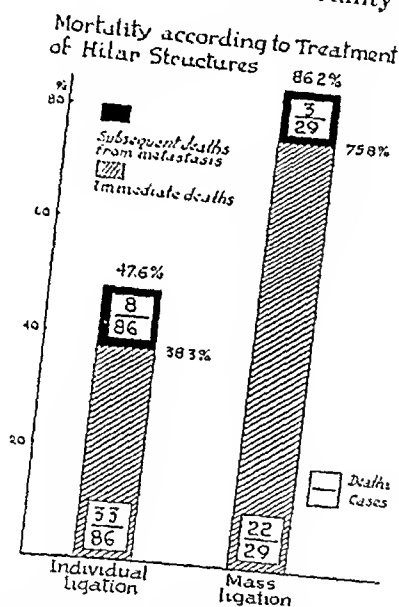


Graph V.—Graphic representation of total mortality in previous and present series of collected cases including our cases.

There are a number of factors which seem to have a significant influence on the mortality in addition to the general condition of the patient and certain technical considerations. The mortality according to sex reveals a lower death rate in females. Of 23 females, 9 (41.6 per cent) died; and of 69 males, 38 (55 per cent) died (Graph I). The exact significance of this fact is difficult to explain. Attention was directed in a previous publication to the fact that the mortality is greater in right-sided lesions. This is further confirmed in the present series. Of 60 right-sided lesions, 27 (45 per cent) died; whereas, of 67 left-sided lesions, 29 (35.8 per cent) died (Graph IV). Technically the operation is more difficult on the right than on the left side, principally due to the fact that on the right side the vena azygos crosses over the eparterial bronchus, usually making mobilization and isolation of the right main stem bronchus difficult. Experimentally it has also been demonstrated that right pneumonectomy is a more serious procedure than left pneumonectomy,⁵⁰ and this has been explained on the basis of greater size and aerating surface of the right

lung. Of significance in this regard is the demonstration of Jacobaeus and his co-workers^{19, 20} by bronchosperometric experiments that the functional capacities of the respective lungs corresponded to the anatomical fact that the right lung constitutes 54 per cent and the left lung 46 per cent of the total volume of both lungs.

The method of treatment of the hilum also influences the prognosis. Of 86 collected cases, including all of ours, in which individual ligation of the hilar structures was done, 33 (38.3 per cent) died; whereas, of 29 collected cases in which mass ligation was used, 22 (75.8 per cent) died (Graph VI). If there are added to these figures subsequent deaths from metastases, the corresponding mortality rates become 47.6 per



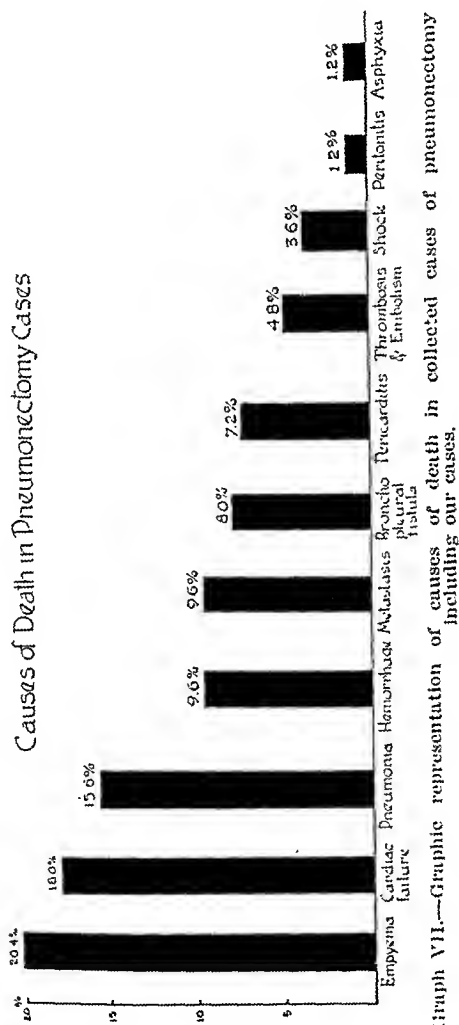
Graph VI.—Graphic representation of mortality according to treatment of hilar structures in 115 collected cases of pneumonectomy including our cases.

cent and 86.2 per cent. These contrasting mortality incidences emphasize further the superiority of individual ligation of the hilar structures over mass ligation.

The causes of death following pneumonectomy are principally due to cardiac and pleuropulmonary complications. In the collected series, including our cases, empyema, cardiac failure, and pneumonia were the most frequent causes of death occurring in incidences of 20.4 per cent, 18 per cent, and 15.6 per cent, respectively (Graph VII). Hemorrhage and metastasis were stated as causes of death in 9.6 per cent each. Bronchopleural fistula was a cause of death in 8 per cent, pericarditis in 7.2 per cent, thrombosis and embolism in 4.8 per cent, shock in 3.6 per cent, and peritonitis and asphyxia in 1.2 per cent each.

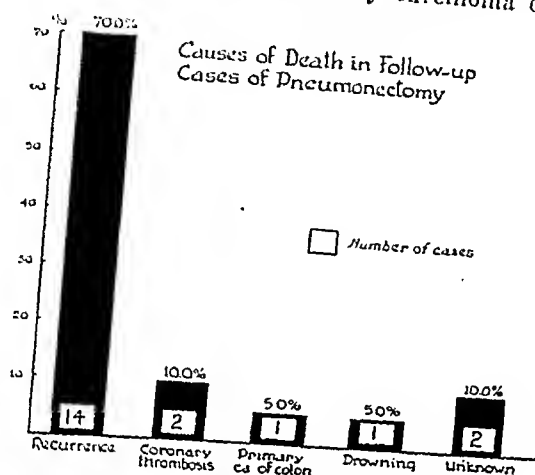
These latter two cases of deaths appeared in our cases and have been referred to in a previous publication.¹¹⁵

Whereas in any surgical procedure the operative mortality is important, in the surgical treatment of malignancy the consideration of follow-up results is of even greater significance. Obviously primary carcinoma of the lung is of too recent development to permit adequate

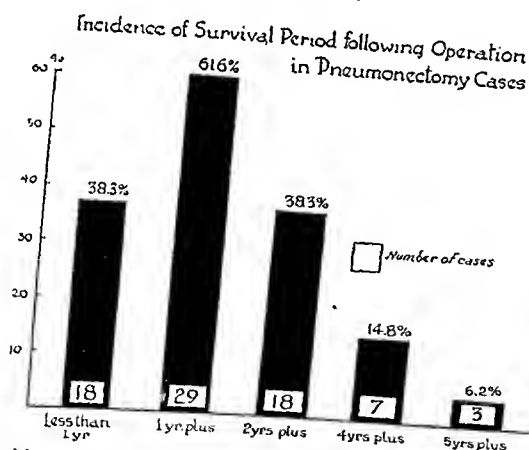


evaluation on the basis of large statistical analyses. It should be realized that the first successful pneumonectomy was done only seven years ago. However, it may be interesting to observe the results of available statistics. Of a series of 83 collected cases, including 10 of ours, which recovered following operation, follow-up data are available in 67. Of this number, 47 (70.1 per cent) were still living at the time of the report and 20 (29.8 per cent) were dead. In our series of 10 recoveries

there have been 3 subsequent deaths, 2 of which were definitely due to recurrence and the third was probably due to a similar cause. These patients survived 10 months, 9 months, and 3 months, respectively. Of the 20 collected cases, including ours, in the follow-up series which died, the cause of death was recurrence in 14 (70 per cent), coronary thrombosis in 2 (10 per cent), primary carcinoma of the colon in 1 (5 per cent), drowning in 1 (5 per cent), and unknown in 2 (10 per cent).



Graph VIII.—Graphic representation of causes of death in 20 collected and our cases with follow-up.



Graph IX.—Graphic representation of incidence of survival periods following operation in 47 collected and our cases with follow-up.

(5 per cent), drowning in 1 (5 per cent), and unknown in 2 (10 per cent). (Graph VIII.) In this group the shortest survival period following operation was 3 months, the longest $3\frac{1}{2}$ years, and the average 1 year. Thirteen cases had survival periods of less than 1 year and 3 cases more than 2 years.

Of the 47 collected cases, including ours, that are still living, 18 (38.3 per cent) have survival periods of less than 1 year and 29 (61.6

per cent) of more than 1 year. Of the latter number, 18 (38.3 per cent) are living 2 years after operation, 7 (14.8 per cent) 4 years after operation, and 3 (6.2 per cent) 5 years after operation (Graph IX). The shortest period is 3 months, the longest 6+ years, and the average 18.8 months. In our series of 7 cases which are still living the survival periods are 4½ years, 2 years, 1½ years, 14 months, 10 months, 8 months, and 7 months.

SUMMARY

1. The increasing interest in carcinoma of the lung is probably due to several factors, among the most important of which are the apparently increasing incidence, the relative frequency, the rapid advances in thoracic surgery, and the demonstrated feasibility of surgical therapy.

2. It is generally agreed that the only curative treatment of primary carcinoma of the lung is surgical extirpation. Irradiation therapy is of little, if any, value and there is some evidence that it may be actually detrimental.

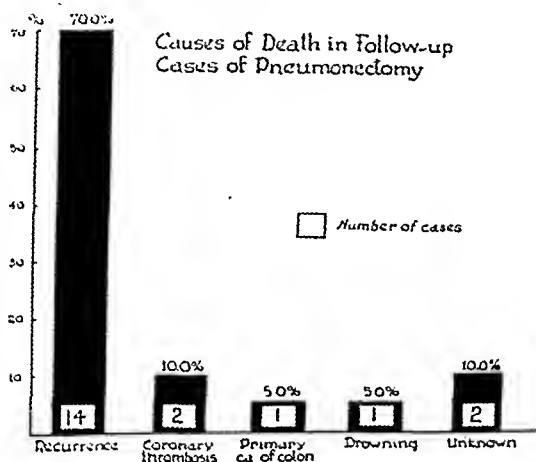
3. Total removal of the involved lung and the mediastinal lymph nodes is the most rational surgical procedure. This can be adequately performed only by individual ligation of the hilar structures.

4. The factors influencing operability in primary carcinoma of the lung are briefly reviewed. Emphasis is placed on the fact that borderline cases should always be given the benefit of exploration, even at the risk of finding a large number inoperable, because it is the only means by which operability can be determined absolutely in these instances. In the collected series 49 per cent were operable and in our series 63.3 per cent were operable.

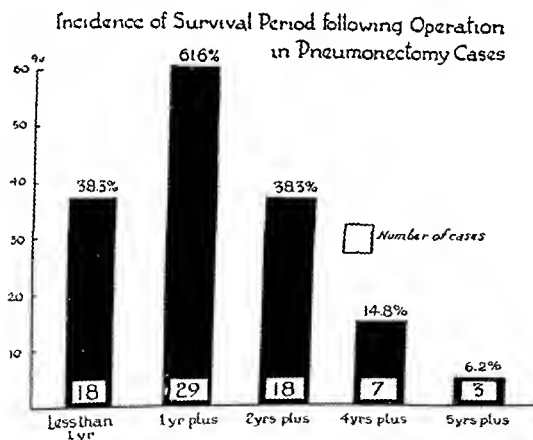
5. The preparatory measures and type of anesthesia in pneumonectomy are discussed. The various approaches used in pneumonectomy are described, illustrated, and evaluated. The technique of exposure, isolation, and individual ligation of the hilar structures is described and illustrated.

6. An analysis of 139 collected and 19 personal cases of total pneumonectomy for neoplastic disease of the lung is presented. The sex incidence showed a predominance of males (75 per cent). The age incidence was highest in the fifth and sixth decades. Primary carcinoma comprised 94 per cent of the cases, primary sarcoma 2.9 per cent, metastatic melanoma 1.5 per cent, metastatic carcinoma 0.7 per cent, metastatic sarcoma 0.7 per cent. Right-sided lesions occurred in 47.2 per cent and left-sided in 52.7 per cent. The general mortality was 45 per cent. The various factors influencing the operative mortality are discussed and critically analyzed. The most frequent causes of death are principally due to cardiac and pleuropulmonary com-

there have been 3 subsequent deaths, 2 of which were definitely due to recurrence and the third was probably due to a similar cause. These patients survived 10 months, 9 months, and 3 months, respectively. Of the 20 collected cases, including ours, in the follow-up series which died, the cause of death was recurrence in 14 (70 per cent), coronary thrombosis in 2 (10 per cent), primary carcinoma of the colon in 1 (5 per cent), drowning in 1 (5 per cent), and unknown in 2 (10 per cent).



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plications. The follow-up results in 67 of 83 collected cases, including ours, are presented. Of this number 70 per cent are still living. In our series 7 of the 10 patients who recovered operation are still living, the longest survival being $4\frac{1}{2}$ years. The average survival period following operation in the collected cases which recovered is 18.8 months.

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Erratum

In the article by Prof. Dr. Eugene Pólya, Budapest, Hungary, entitled "Simple Apparatus for the Relief of Some Palsies of the Upper Extremities" which appeared in the September issue of the *JOURNAL*, the plate upon which appear Figs. 1, 2, and 3 has been printed upside down, thus reversing the figures. The legends are correct if the reader will consider the plate inverted.

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association of the names of individuals with titles of diseases, I believe the expression, Ludwig's angina is going to exist for many more years to come.

When one reviews the various mortality percentages associated with the treatment of this disease, there can be but one conclusion reached; namely, there must be at the present time a very wide difference of opinion as to what actually constitutes a case of von Ludwig's angina, for there is not sufficient difference to be found in the various methods of treatment advocated to explain the wide difference of mortality statistics, the lowest of these mortality statistics reported being 5 per cent, and the highest 74 per cent. For this reason, it might be interesting to quote the requirements that Ludwig himself thought necessary in order to establish the diagnosis of Ludwig's angina. These were:

"1. There should be inflammation of the deep cellular tissues under the tongue.

"2. This inflammation should begin around the submaxillary salivary gland.

"3. This inflammation should subsequently invade the neck and the floor of the mouth.

"4. That this condition should run a course which grows progressively worse with death in ten to twelve days or gradual recovery."

This description of the condition is sufficiently indefinite to explain the present-day mental confusion regarding what actually constitutes the diagnosis of von Ludwig's angina. It also makes us wonder as to how much the great popularity of Queen Catherine had to do with the continuation of the use of this name.

A recent compilation of statistics from various reports in literature in which the cause was mentioned reveals that extraction of the lower molar teeth preceded the beginning of infections in the deep structures of the tongue in 82 per cent of cases. Calculus in the duct of the submaxillary salivary gland, fracture of lower mandible through abscess cavities, injury from foreign bodies in mouth, etc., have also been found as etiologic factors.

The explanation of the frequency with which these deep infections follow extractions of the lower molars is to be found in the fact that the lower molars are set off center and toward the tongue in the mandible bone. The remaining teeth are also set off center but toward the outer (labial) side. This anatomical difference explains why infection of the deep structures under the tongue takes place more readily through the thin bony partition on the inner side than through the thick outer side of the mandible following extraction of the lower molars. The reverse is true as regards the relationship of the remainder of the teeth. For this reason, infections following extractions of the anterior teeth are more apt to originate through the thin outer partition than they are to perforate through the thicker inner partition.

Editorial

Von Ludwig's Angina

A LITTLE over a century ago (1836) an unusually popular queen died. Her death was due to what was then described as a "sublingual phlegmon." This was Queen Catherine of Württemberg. It is natural to presume the cause of her death was then fully discussed by both the laity and by the medical profession. Shortly after Queen Catherine's death, Professor Wilhelm Friedrich von Ludwig (1790-1865), Vice Director and Liebartz of Stuttgart, made an address before a medical group assembled in that city. It is not surprising that he selected as the subject of his address the cause of the recent death of their beloved queen. Ludwig must have made a most impressive and illuminating explanation of the disease, as a year later Camerer gave the title of "von Ludwig's angina" to the condition, and, as such, it has now been known for over one hundred years.

In 1892 there was a debate between Delorme and Nélaton relative to the propriety of retaining Ludwig's name in association with this disease.

Again in 1929, Ashhurst, in an address as the invited guest of the Western Surgical Association on the subject of "Ludwig's Angina," stated that the medical profession in its attitude toward the retention of any doctor's name in association with a disease was largely divided into two groups: The first, those who followed the teachings of Hippocrates in objecting to the unnecessary multiplication of names of diseases and preferred to assign the so-called "new diseases" to their proper places under already recognized pathologic processes; the second group, the Cridians (of whom I had never heard until I read Ashhurst's address). With them, every new symptom and every new complication constitutes a new disease.

It is interesting to recall that Ludwig's angle, that angle situated between the manubrium and the gladiolus, derived its name from Daniel Ludwig (1625-1680), a German anatomist. Furthermore, Ludwig's ganglion, a ganglion connected with the cardiac plexus and situated near the right auricle of the heart, obtained its name from still a different Ludwig; namely, Karl Friedrich Wilhelm Ludwig, of Leipzig, a German physiologist (1816-1899). However, Karl Friedrich Wilhelm Ludwig's name is not attached to any of the many recording instruments which he introduced into physiology.

The expression "von Ludwig's angina" is with us today, and no matter what our individual views might be concerning the propriety of the

Book Reviews

The Pineal Organ: The Comparative Anatomy of Median and Lateral Eyes, With Special Reference to the Origin of the Pineal Body; and a Description of the Human Pineal Organ Considered From the Clinical and Surgical Standpoints. By R. J. Gladstone and C. P. G. Wakeley. Baltimore, 1940. Williams & Wilkins Co. Pp. 528, with 324 figures. \$10.

This volume, written by a well-known London anatomist and embryologist and by a neurosurgeon, was prepared because its authors had found that the investigation of pineal tumors had proved rather fruitless, and they therefore "determined to investigate the whole question of the nature of the pineal organ from the lowest to the highest forms in the animal kingdom." Once embarked upon this stimulating project, they soon discovered that, in order to assess the true significance of facts which have been observed in connection with the mammalian epiphysis, it would be necessary to investigate the history of the pineal body and parietal sense organ from the standpoints of embryology, comparative anatomy, and paleontology. As Sir Arthur Keith points out in his introductory chapter, Gladstone, in tracing the origin and evolution of the human pineal, has gone back over a period of some four hundred million years, when median as well as lateral eyes had appeared on the head of our invertebrate ancestors. By comparing evidence from fossil remains and also from living creatures through the animal kingdom, a convincing story has been written of the way this structure attained the position of a visual organ with a lens, retina, and nervous stalk, and then, with the development of efficient lateral eyes, has retrogressed to its present unimportant position. The authors attempt to push back the origin of the pineal organ to the median eyes seen in many invertebrates. This possibility was first suggested by Gaskell, who did pioneer work on the pineal as well as on the autonomic nervous system. A double pineal stalk is present in certain forms of eels which is connected by nonmyelinated fibers with the habenular ganglia, and thence by the retroflex bundle of Meynert and stria medullaris with the olfactory apparatus. All these structures make up the epithalamus and may have formerly been concerned with feeding reflexes. Fusion of the paired earlier structures occurs in higher species of vertebrates, with retrogression of one side and its underlying nervous connections. In the eyclostomes (a primitive order of round-mouthed fishes, such as the lamprey eels and hag fish) the pineal eye may still act as a visual organ, although devoid of a lens. In the lizard the pineal organ lies just beneath the skin with central nervous connections which run through a foramen in the skull, but it is doubtful if this apparatus is sensitive to light. The same arrangement persists in tadpoles, but in adult frogs the nervous stalk is cut off by the cranial vault and only a spot of pigment is left beneath the skin. Only vestiges of the parietal sense organ and its stalk remain in the more primitive mammalian embryos and in the adult forms nothing but the basal segment of the pineal organ, the conarium, persists. The chapter on the pineal system of mammals omits interesting data on comparative anatomy, more especially the important contributions of Krabbe (1921, 1925, and 1929) and the studies of the pineal apparatus of marine mammals by Fuse (1936).

In the final third of the book physiologic evidence is reviewed, which shows that the mammalian pineal has not actually undergone metamorphosis into a gland of eternal secretion, but that the apparent endocrine changes produced by

In addition to these differences in skeletal structure the firm attachment of the deep cervical fascia and the mylohyoid muscle to the lower inner edge of the inferior mandible confines infections, rupturing through the inner side of the bone to the deep structures. When the infection through the bone ruptures to the outer side of the mandible, this fascia and muscle tend to confine the inflammation to the superficial structures.

For these reasons, infections following extractions of the anterior teeth are not apt to be as serious as those following the removal of the lower molars. If infection following extractions of the anterior group of teeth does not subside quickly, superficial fluctuation soon develops without general symptoms and the pus is easily released. Such a picture is the reverse of what is seen in infections of the deep structures under the tongue.

The use of sulfanilamide and its various derivatives can be employed to great advantage before the extraction of lower molars, especially if there is any infection present.

Cultures of the infected gums and, if possible, of the abscess associated with the teeth should be a basis of selection of which one of the sulfanilamide compounds should be employed.

After extraction of unerupted teeth, zinc peroxide, as prepared by Meleney's method, has proved of benefit in preventing postextraction infections. In such cases there is frequently found an ulcer on the undersurface of the gum which has to be incised in order to expose the tooth. An anaerobic hemolytic streptococcus is usually present in such ulcers.

The closest possible cooperation between dentist and surgeon is imperative. If a hard painful swelling develops under the tongue after the extraction of a lower molar, incision and drainage should be instituted at an early period. One should not wait for the fluctuation which does not usually occur and, of course, should not postpone surgical relief until the patient is partially strangled.

If the tension of tissues is sufficiently great to produce elevation of the hyoid bone, the fibers of the mylohyoid muscle should be cut transversely so as to give almost immediate relief from the "pull" on the trachea. Necrotic material, and, if indicated, the submaxillary salivary gland should be removed. In fact, everything should be done in order to release the tongue quickly from obstructing the air passages to the lung.

The most satisfactory incision in extreme cases is the one about one-half inch from the lower edge of the mandible, extending from one angle of the jaw to the other angle. Of course, in order to obtain relief it is necessary to incise widely the deep cervical fascia as well as to divide the mylohyoid muscle transversely.

A preliminary tracheotomy done with local anesthesia is sometimes indicated and, when done, the opening in the trachea can be used for a gas anesthetic of the surgeon's choice.

Book Reviews

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In the final third of the book physiologic evidence is reviewed, which shows that the mammalian pineal has not actually undergone metamorphosis into a gland of eternal secretion, but that the apparent endocrine changes produced by

certain pineal tumors, such as pubertus precox, in reality are due to compression of the hypothalamus. The surgical chapters include the pathology of pineal tumors, their symptomatology, clinical case histories, and operative technique. The chapter on symptomatology, especially the explanation of the characteristic limitation of eye movements, is particularly well done; but the chapter on case histories is brief and references to many cases of outstanding interest which have been reported in the literature are not included. As a result it is not possible to obtain an accurate impression of the life history of these tumors, or to define the operative risk involved in attempts at their extirpation, or to be certain about the amount of improvement that can be expected from radiation.

In evaluating the book, the comparative anatomical chapters, which make up its major portion, and its illustrations deserve the highest praise. From the more specialized viewpoint of the neurosurgeon, rather than from that of the comparative anatomist, this portion is too long and detailed, so that one cannot help feeling that condensation of the first 380 pages would clarify the evolutionary history. The glossary could well be enlarged, so that the surgeon who has not had an extensive zoological training could identify species such as *Petromyzon*, *Lacerta*, etc. In the bibliography, since the method has been adopted of listing the articles by title, one wishes that this had been carried throughout consistently.

The Pathology of Internal Diseases. By William Boyd. Ed. 3. Cloth. Pp. 874, with 357 illustrations. Philadelphia, 1940, Lea and Febiger. \$10.

This authoritative work, which first appeared in 1931, has been thoroughly revised and recent advances in internal medicine have been added. In the preface to the first edition the author stated that it was his purpose to correlate the symptomatology of disease with the pathologic lesions. He succeeded admirably in integrating pathology with internal medicine. The present edition includes new material on diseases of the heart, vitamin K, bronchogenic carcinoma, the relation of the pituitary to pancreatic diabetes, the anemias, renal diseases, and silicosis. While many sections have been rewritten and new material added, the number of pages remains approximately the same. Several new illustrations have been introduced, including four colored plates, all of which are appropriate to the text and are well reproduced.

Many factors have contributed to the success of this textbook. The author is a master of English prose. He constantly refers to and quotes passages from the medical literature pertaining to the subject under discussion. As an example, he presents Bright's own account of the clinical course of nephritis. In developing each section, a concise but lucid description of the normal histology and physiology is given, followed by a consideration of the morbid anatomy and its relation to symptoms. Well-selected references to the literature conclude each chapter.

A delightful feature of this book is the manner in which the pathogenesis of various diseases is presented. If controversial subject matter is discussed, the author cites the outstanding contributions on both sides and then develops his own opinion. In an inquiry into the pathogenesis of tuberculosis he terminates the discussion with the statement: "Immunity is the master word in tuberculosis. It is more to be desired than freedom from infection, for the latter is an unattainable ideal, and the rarer the infection, the more dangerous does it become." This assertion will be challenged by many. Again in a consideration of the pathogenesis of hyperthyroidism, he maintains that it is a mistake to separate

toxic adenoma from exophthalmic goiter: "Both should be included under the heading of Grave's disease. The adenoma is a mere incident in the course of the pathological process." The section on jaundice is excellent. Exception must be taken to one statement. In discussing the chromaffin cell tumor, also known as pheochromocytoma, he writes: "It is quite innocent, perfectly encapsulated, usually of small size, and may be found in elderly persons at autopsy by accident." It is now recognized that these benign-appearing tumors may secrete enough adrenalin to cause death.

This textbook is highly recommended to the medical student who has completed the introductory courses in internal medicine and pathology. It can be read with profit by every teacher and practitioner.

Die Entzündungsbestrahlung. By Dr. Med. Habil. R. Glauner. Paper. Pp. 190, with 14 illustrations and 14 tables. Leipzig, 1940, George Thieme. RM 15.

This monograph attempts to cover in a comprehensive manner the subject of inflammation treated by x-ray radiation. The book is divided into two parts. The histological, chemical, and physiological effects of x-ray radiation of inflamed tissues are considered in detail in the first portion. The second portion deals with the effects of roentgen therapy of inflammatory processes in various organs of the body. The world's medical literature on the subject has been painstakingly reviewed and admirably summarized. There is little that is original in the book, the author's contribution being chiefly his interpretation of the work of others and the recital of his results in the treatment of various inflammatory lesions with x-ray radiation. An extensive bibliography and a satisfactory index are appended.

The surgeon or general practitioner will hardly find it worth his while to purchase or read this book. It has a definite place, however, as a reference book and those in the profession particularly interested in roentgen therapy may find it valuable.

The Head and Neck in Roentgen Diagnosis. By Henry K. Paneoast, M.D., Late Professor of Radiology and Director of the Department of Radiology, University of Pennsylvania; Eugene P. Pendergrass, M.D., Professor of Radiology and Director of the Department of Radiology, University of Pennsylvania; and J. Parsons Schaeffer, M.D., Ph.D., Professor of Anatomy and Director of the Daniel Baugh Institute of Anatomy, Jefferson Medical College. Pp. 976, with 1,251 figures. Springfield, Ill., 1940, Charles C. Thomas, Publisher. \$12.50.

In no region of the body is the anatomy more complex than in the head and neck. It is particularly fitting therefore that a dissertation on the roentgenology of this region should be based upon the concept of roentgen diagnosis as a visual presentation of gross anatomy, both normal and pathologic. This volume stands out as a splendid example of the results which may be achieved by a collaboration of the roentgenologist and the anatomist in the preparation of texts on roentgen diagnosis. The authors have covered the roentgen diagnosis of a series of diverse but grossly related structures in most admirable fashion. Practically all of the well-established data related to the roentgen examination of the skull and its contents, the various facial bones, the paranasal sinuses and mastoids with their associated structures, the jaws and the teeth, the cervical spine, the upper respiratory tract and the neck are in this detailed and well-ordered treatise.

For each structure there is a consideration of the normal gross anatomy and its variations, the normal roentgen anatomy, the technique of x-ray examination, and finally the roentgen diagnosis of disease processes. While the authors have drawn largely from their own rich experience, sufficient attention has been paid to the contribution of others. Each chapter contains a bibliography which, while not voluminous, is sufficient to give the references for almost all the subjects which are not fully covered in the book itself. The illustrations are unusually numerous, some 1,251 figures being exhibited. They are splendidly chosen, well arranged for accessibility and clearly labeled; many exceptionally fine anatomical figures are included. While the cuts are not as brilliant in detail as might be desired, with few exceptions they demonstrate all that is needed. The section on intracranial tumors and cerebral pneumography is especially well done. Some doubt may be held as to the lack of final proof of some of the cases presented, but in most instances there is no question as to the findings. The material in this book is much too extensive to permit detailed criticism; the reputation of the authors is sufficient to warrant the authenticity of the data. Considering the size of the book, the number of errors in the first printing is small. Attention should be directed to the transposition of Figs. 701 and 703 and to a few typographical errors in spelling. The publisher is to be commended for the format, the printing, the generous number of figures, and particularly for the reasonable price put upon so large and fine a volume. This is no doubt the most authoritative and most complete reference work we have on this subject; it will be indispensable to the roentgenologist, the neurosurgeon, the neurologist, the otolaryngologist, in fact to any physician concerned with the diagnosis of the diseases of the head and neck. It will remain permanently as a fitting memorial to the memory of the distinguished senior author.

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